```
     FILE 'CAPLUS, WPIDS' ENTERED AT 21:07:49 ON 18 JAN 2005
L1         4139 S NITRIC OXIDE (100A) (NITRITE# OR NITRATE#)
L2       366518 S (TWO OR SEPARAT? OR MULTI# OR SEVERAL OR MULTIPLE OR TWIN OR
L3            9 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 21:11:00 ON 18 JAN 2005

     FILE 'CAPLUS, WPIDS, MEDLINE' ENTERED AT 21:13:58 ON 18 JAN 2005
L4         6335 S NITRIC OXIDE (100A) (NITRITE# OR NITRATE#)
L5           59 S L4 AND ((NITRIC OXIDE OR NITRATE# OR NITRITE#) (25A) (CREAM#
L6           46 DUP REM L5 (13 DUPLICATES REMOVED)
L7           43 S L6 NOT L3

     FILE 'STNGUIDE' ENTERED AT 21:15:45 ON 18 JAN 2005

=> d que l3; d que l7
L1         4139 SEA NITRIC OXIDE (100A) (NITRITE# OR NITRATE#)
L2       366518 SEA (TWO OR SEPARAT? OR MULTI# OR SEVERAL OR MULTIPLE OR TWIN
                  OR DISCRETE) (10A) (PART# OR CONTAINER# OR GEL# OR PACKAG? OR
                  PACK#)
L3            9 SEA L1 AND L2



L1         4139 SEA NITRIC OXIDE (100A) (NITRITE# OR NITRATE#)
L2       366518 SEA (TWO OR SEPARAT? OR MULTI# OR SEVERAL OR MULTIPLE OR TWIN
                  OR DISCRETE) (10A) (PART# OR CONTAINER# OR GEL# OR PACKAG? OR
                  PACK#)
L3            9 SEA L1 AND L2
L4         6335 SEA NITRIC OXIDE (100A) (NITRITE# OR NITRATE#)
L5           59 SEA L4 AND ((NITRIC OXIDE OR NITRATE# OR NITRITE#) (25A)
                  (CREAM# OR GEL# OR LOTION# OR TOPICAL?))
L6           46 DUP REM L5 (13 DUPLICATES REMOVED)
L7           43 SEA L6 NOT L3
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L3 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:561963 CAPLUS
TI Controlled release of nitric oxide from electrospun nanofiber transdermal matrices
AU Bhide, Mahesh
CS University of Akron, Akron, OH, USA
SO Abstracts, 35th Great Lakes Regional Meeting of the American Chemical Society, Chicago, IL, United States, May 31-June 2 (2003), 251 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69EBCS
DT Conference; Meeting Abstract
LA English
AB **Nitric oxide**, generated by the reaction of ascorbic acid and **nitrite**, shows promise for the treatment of warts and parasitic lesions. Previously methods have been devised to maintain, stabilize and sequester the two reagents in various simple transdermal delivery devices. These methods make use of **two**-component creams, ointments, and **gels** contg. either nitrite or ascorbic acid, which requires thorough mixing prior to use. Microcapsulation of these two active reagents in a single delivery system may provide long term stability of the reagents, and reproducible and predictable controlled release of nitric oxide. Electrospinning is a fabrication process that uses an elec. field to control the deposition of polymeric nanofibers. This simple, rapid, and efficient method can be used for encapsulation of sol. additives and/or entrapment of insol. particles in polymeric nanofiber matrixes. Sandwiched, nanofiber matrixes A and B were electrospun from ethanol contg. the following four equal layers. Matrix A: 1. hydrophilic polyurethane elastomer, Water lock super absorbent [10:1.5(wt./wt.)], 2. hydrophilic polyurethane elastomer, ascorbic acid [10:1.8 (wt./wt.)], 3. hydrophilic urethane elastomer, Water lock super absorbent [10:1.5 (wt./wt.)], 4. hydrophilic polyurethane elastomer, anion exchange resin-nitrite form [10:0.9(wt./wt.)]. Matrix B: transdermal layers 1 and 3: hydrophilic polyurethane elastomer, Water lock super absorbent [10:2.5 (wt./wt.)]. Matrixes A and B rapidly absorb 380% and 600% water resp. forming strong, elastomeric hydrogels which immediately release **nitric oxide**. **Nitric oxide**, measured as headspace gas from hydrated matrixes, shows first order kinetics with the yield of 25-30% based on available **nitrite** on the resin. The half-life of nitric oxide obsd. for these matrixes are 1.3 h and 2.8 h. at 230C resp. These nanofiber sandwiched matrixes provide a stable, dry storage form for these two reagents, which upon hydration produces a hydrogel transdermal device for the controlled delivery of nitric oxide.

L3 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:426236 CAPLUS
DN 137:41640
TI Study of a combined percutaneous local anaesthetic and nitric oxide-generating system for venepuncture
AU Tucker, A. T.; Makings, E.; Benjamin, N.
CS The Ernest D. Cooke Clinical Microvascular Unit, St. Bartholomew's Hospital, London, EC1A 7BE, UK
SO Anaesthesia (2002), 57(5), 429-433
CODEN: ANASAB; ISSN: 0003-2409
PB Blackwell Science Ltd.
DT Journal
LA English
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB **Nitric oxide** (NO) may be generated and delivered into the skin via a novel system of sodium **nitrite** and ascorbic acid.

This placebo-controlled, double-blind trial compared the analgesic properties of this system alone and when supplemented with lidocaine. The pain of dorsal hand vein cannulation was assessed in 100 volunteers. The NO-generating system was prepd. by mixing **two gels,** the first KY jelly and sodium nitrite (10% w/v), the second KY jelly and ascorbic acid (10% w/v). NO-generating gel was the placebo treatment, and when combined with lidocaine (final concn. 5%), formed the active treatment. The gels were applied to the dorsum of the hands bilaterally and simultaneously for 10 min. Following cannulation, pain perception was measured with a verbal rating score (VRS) and a visual analog score (VAS). The active formulation significantly decreased the VRS ($p < 0.0001$) and also reduced the mean VAS by > 40% compared with placebo ($p < 0.001$). This investigation suggests a 10-min topical application of anesthetic combined with the NO-generation system may provide effective analgesia for venous cannulation in adults.

ST lidocaine ascorbate **nitrite** anesthetic analgesic **nitric oxide** venipuncture pain

IT 50-81-7, Ascorbic acid, biological studies 137-58-6, Lidocaine 7632-00-0, Sodium **nitrite**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined percutaneous local anesthetic and **nitric oxide**-generating system for venipuncture)

L3 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:215136 CAPLUS
DN 136:382018
TI Nitric Oxide in Biological Denitrification: Fe/Cu Metalloenzyme and Metal Complex NOx Redox Chemistry
AU Wasser, Ian M.; de Vries, Simon; Moeenne-Loccoz, Pierre; Schroeder, Imke; Karlin, Kenneth D.
CS Department of Chemistry, The Johns Hopkins University, Baltimore, MD, 21218, USA
SO Chemical Reviews (Washington, D. C.) (2002), 102(4), 1201-1234
CODEN: CHREAY; ISSN: 0009-2665
PB American Chemical Society
DT Journal; General Review
LA English
RE.CNT 333 THERE ARE 333 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A review. A different form of denitrification yielding nitrous oxide (N_2O) as the end product from nitrate (NO_3^-) or nitrite (NO_2^-) is catalyzed in the mitochondria of several fungi and yeasts. In bacteria and archaea, each of the four redn. steps is catalyzed by one (or more) distinct metalloenzyme complexes, employing various transition metals (Mo, Fe, Cu) that are found in varying ligand environments (i.e. heme, histidine ligation, sulfide ligation, etc.). Over the past years, it has become evident that nitric oxide (NO) is a compulsory intermediate in bacterial denitrification. The study of bacterial NO-binding (and -releasing) enzymes and relevant model complexes might provide valuable structural, spectroscopic, and mechanistic information also relevant to other important NO-binding enzymes. Therefore, it is of great interest to study both the metalloenzymes that produce NO from **nitrite,** **nitrite** reductase (NIR), and also the metalloenzymes that reduce NO to nitrous oxide, **nitric oxide** reductase (NOR). This review has a **two-part** focus, following an initial introductory section on relevant bioenergetics: (1) an examn. of metalloenzyme reactivity with NO, specifically, metalloenzymes that both produce NO from **nitrite** (**nitrite** reductases) and those that reduce NO to nitrous oxide (**nitric oxide** reductases); and (2) a review of the inorg. coordination complex reactivity with NO, including Cu-NOx and Fe-NOx redox chemistries, since

these metals are cofactors for the NO-producing (NIR) and NO-consuming (NOR) enzymes.

ST review **nitrite** reductase denitrification **nitric oxide** metalloenzyme

L3 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:111834 CAPLUS
DN 137:92531
TI Treatment of Crohn's disease with recombinant human interleukin 10 induces the proinflammatory cytokine interferon .gamma.
AU Tilg, H.; van Montfrans, C.; van den Ende, A.; Kaser, A.; van Deventer, S. J. H.; Schreiber, S.; Gregor, M.; Ludwiczek, O.; Rutgeerts, P.; Gasche, C.; Koningsberger, J. C.; Abreu, L.; Kuhn, I.; Cohard, M.; LeBeaut, A.; Grint, P.; Weiss, G.
CS Department of Medicine, Division of Gastroenterology and Hepatology, University Hospital Innsbruck, Innsbruck, 6020, Austria
SO Gut (2002), 50(2), 191-195
CODEN: GUTTAK; ISSN: 0017-5749
PB BMJ Publishing Group
DT Journal
LA English
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Background: Interleukin 10 (IL-10) exerts anti-inflammatory actions by counteracting many biol. effects of interferon .gamma. (IFN-.gamma.). Aims: To investigate this in humans, we studied the effects of human recombinant IL-10 administration on IFN-.gamma. prodn. by patient leukocytes. Furthermore, we assessed the IFN-.gamma. inducible mol. neopterin and **nitrite/nitrate** serum levels, which are indicative of endogenous **nitric oxide** formation. Methods: As **part** of **two** placebo controlled double blind studies, we analyzed patients with chronic active Crohn's disease (CACD) who received either s.c. recombinant human IL-10 (n=44) or placebo (n=10) daily for 28 days, and patients with mild to moderate Crohn's disease (MCD) treated with either s.c. IL-10 (n=52) or placebo (n=16) daily for 28 days. Neopterin and nitrite/nitrate concns. were measured in serum, and ex vivo IFN-.gamma. formation by lipopolysaccharide or phytohaemagglutinin (PHA) stimulated whole blood cells were investigated before, during, and after IL-10 therapy. Results: In patients with CACD, the highest dose of 20 .mu.g/kg IL-10 caused a significant increase in serum neopterin on days + 15 and + 29 of therapy compared with pretreatment levels. No changes were obsd. for nitrite/nitrate levels under either condition. In MCD, treatment with 20 .mu.g/kg IL-10 resulted in a significant increase in PHA induced IFN-.gamma. prodn. Conclusions: High doses of IL-10 upregulate the prodn. of IFN-.gamma. and neopterin. This phenomenon may be responsible for the lack of efficacy of high doses of IL-10 in the treatment of CACD and MCD.

L3 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:562528 CAPLUS
DN 133:168389
TI Systems and methods for topical treatment with nitric oxide
IN Seitz, William A.; Garfield, Robert E.; Balaban, Alexandru T.; Stewart, Randall J.
PA Nitric Oxide Solutions, USA
SO U.S., 16 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 6103275 A 20000815 US 1998-95174 19980610
CA 2410990 AA 20011129 CA 2000-2410990 20000524
WO 2001089572 A1 20011129 WO 2000-US14239 20000524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
EP 1283724 A1 20030219 EP 2000-932745 20000524
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI US 1998-95174 A2 19980610
WO 2000-US14239 W 20000524
RE.CNT 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB A simple, biocompatible system and procedure for generating nitric oxide (NO) is described. A mixt. of powd. sodium **nitrite**, ascorbic acid, and maleic acid (or another org. acid of adequate strength) immediately generates **nitric oxide** (NO) on treatment with water. To slow down the NO generation, one may prep. an ointment from a nonaq. medium (petrolatum, vaseline) and the three powd. ingredients, which on being applied topically on the skin will release NO as water permeates through this medium; alternatively, one may convert the aq. sodium nitrite soln. into a gel with hydroxyethylcellulose (or other gel-forming compd.) and combine this gel with another gel obtained from aq. ascorbic and maleic acids with hydroxyethyl cellulose for topical application (on intact skin, burns, intra-cavity, etc.). The **two gels** may be admixed immediately before use (possibly from a single container with sep. chambers and dual nozzle, via pushing or squeezing the **two gels** through the nozzle), or may be applied in sandwich-like fashion (possibly as a transdermal patch) for further slowing down the delivery of NO.

IT 50-81-7, Ascorbic acid, biological studies 59-02-9, .alpha.-Tocopherol 89-65-6, Erythorbic acid 110-16-7, Maleic acid., biological studies 7632-00-0, Sodium **nitrite**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nitric oxide**-generating systems for promoting tissue healing)

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:455 CAPLUS
DN 130:181714
TI Effect of erythorbate on the acceleration of color formation in meat products
AU Sakata, Ryoichi
CS School of Veterinary Medicine, Azabu University, Japan
SO Erisorubinsan no Kenkyu (1998), 4, 37-42
CODEN: ERKEFS
PB Erisorubinsan Kenkyukai
DT Journal
LA Japanese

AB Warming is known as a meat processing technol. In this treatment, the meat is warmed to a medium temp. after curing, then dried and smoked. Through this process, color, flavor and rheol. properties of meat products are known to improve. This warming seems to cause an aging process. Since the last 2 yr in Europe, erythorbate has been permitted to be used as an antioxidant. Erythorbate appears to produce **nitric oxide** from **nitrite** more efficiently, and also the color formation is accelerated. Research was carried out on the addn. of erythorbate and the combination effect of warming of meat products. The

porcine meat (24 h postmortem) was minced and NaCl (2%) plus NaNO2 (100 ppm) were added, and vacuum packed to be cured. Sodium erythorbate (NaEry) was added to a level of 0.055%. The sample including 0.05% of sodium ascorbate (NaAsc) was prepd. for comparison. After **several** days, each 100 g was stuffed into vacuum **packs**, plastic casings (Krehalon film) and/or hog casings. The samples were then warmed in a water bath or in a smoke house at 50.degree.C. In the smoke house, the relative humidity (RH) was controlled at 80%. After reaching 37-40.degree.C in the center of the meat samples, they were then cooked at 75 .degree.C for 1 h. The color forming ratio, discoloration extent against light exposure, Hunter value and residual nitrite were detd. By warming with the addn. of NaEry or NaAsc, the color tended to increase in both cases. When the warming time increased, the color showed no difference compared with the control sample. In the expt. with natural hog casings, the sausage sample with 80% RH reached more quickly the intended temp. compared with the case of 70% RH, and showed a better color. Under the light exposure with circa 2,500 Lx, the inhibitory effect of the combined erythorbate and warming showed as discoloration. In this expt., the difference of the residual nitrite level with and without warming could not be detected. Both the NaEry and NaAsc decreased the nitric level, however the significant difference among these agents could not be obsd.

L3 ANSWER 7 OF 9 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-564594 [52] WPIDS
DNC C2000-168113
TI Topical controlled release **nitric oxide** composition useful for enhancing local blood flow, comprises **nitrite** salt, acid and biocompatible reductant.
DC B06
IN BALABAN, A T; GARFIELD, R E; SEITZ, W A; STEWART, R J
PA (NITR-N) NITRIC OXIDE SOLUTIONS
CYC 90
PI US 6103275 A 20000815 (200052)* 16
WO 2001089572 A1 20011129 (200202)# EN
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000050426 A 20011203 (200221)#
EP 1283724 A1 20030219 (200321)# EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT US 6103275 A US 1998-95174 19980610; WO 2001089572 A1 WO 2000-US14239 20000524; AU 2000050426 A AU 2000-50426 20000524, WO 2000-US14239 20000524; EP 1283724 A1 EP 2000-932745 20000524, WO 2000-US14239 20000524
FDT AU 2000050426 A Based on WO 2001089572; EP 1283724 A1 Based on WO 2001089572
PRAI US 1998-95174 19980610; WO 2000-US14239 20000524;
AU 2000-50426 20000524; EP 2000-932745 20000524
TI Topical controlled release **nitric oxide** composition useful for enhancing local blood flow, comprises **nitrite** salt, acid and biocompatible reductant.
AB US 6103275 A UPAB: 20001018
NOVELTY - Controlled release topical composition comprises **two** aqueous **gels**. The first **gel** comprises a nitrite salt and the second gel comprises an acid with pKa of 1-4. At least one of the gels comprises a biocompatible reductant.
ACTIVITY - Vulnerary; dermatological; hair growth stimulant; vasodilator; bronchodilator.
MECHANISM OF ACTION - Localized nitric oxide release.

USE - Useful in treatment of hypertension, angina, atherosclerosis and pre-eclampsia and the regulation of vascular conductance, blood flow and blood pressure. The composition is also useful for altering gastrointestinal motility and treating pyloric stenosis; for treating asthma, pulmonary hypertension and improving lung function in premature babies; treating inflammatory diseases, autoimmune diseases, cancer, anaphylactic shock and allograft rejection; diabetes; menstrual and female reproductive disorders; as a female contraceptive; for treating impotence and prostate hypertrophy and other male reproductive system disorders; incontinence; renal arterial stenosis; dermal problems including eczema, acne topical hair loss and wound care and for treating burn injuries.

ADVANTAGE - None given.

Dwg.0/7

TT TT: TOPICAL CONTROL RELEASE **NITRIC OXIDE** COMPOSITION USEFUL ENHANCE LOCAL BLOOD FLOW COMPRISE **NITRITE** SALT ACID BIOCOMPATIBLE REDUCE.

L3 ANSWER 8 OF 9 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2000-237729 [20] WPIDS
CR 2000-237774 [20]
DNC C2000-072395
TI Xanthine oxidoreductase compositions, normally buttermilk based, for prevention of bacterial gastrointestinal disorders, particularly in babies, enteral fed adults, and young animals.
DC B04 C03 D13 D16
IN BLAKE, D R; EDWARDS, R; EISENTHAL, R; HARRISON, R; MILLAR, T M; STEVENS, C R; MILLER, T M; EDWARD, R
PA (UYBA-N) UNIV BATH
CYC 89
PI WO 2000011965 A2 20000309 (200020)* EN 41
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9955264 A 20000321 (200031)
EP 1143808 A2 20011017 (200169) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
GB 2370486 A 20020703 (200251)
ZA 2001002372 A 20021127 (200305)# 61
US 2004120938 A1 20040624 (200442)
ADT WO 2000011965 A2 WO 1999-GB2845 19990827; AU 9955264 A AU 1999-55264 19990827; EP 1143808 A2 EP 1999-941769 19990827, WO 1999-GB2845 19990827; GB 2370486 A WO 1999-GB2845 19990827, GB 2001-6182 20010313; ZA 2001002372 A ZA 2001-2372 20010322; US 2004120938 A1 Cont of WO 1999-GB2845 19990827, Cont of US 2001-763791 20010425, US 2003-732679 20031210
FDT AU 9955264 A Based on WO 2000011965; EP 1143808 A2 Based on WO 2000011965; GB 2370486 A Based on WO 2000011965
PRAI GB 1998-27243 19981210; GB 1998-18913 19980828; ZA 2001-2372 20010322
AB WO 200011965 A UPAB: 20040702
NOVELTY - A formulation including active xanthine oxidoreductase (XOR), for use as a bactericidal agent in the human or other animal digestive system.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a combination product for use in the preparation of the novel formulation, the product comprising a portion of active XOR and a portion of no active XOR;

(2) a composition for addition to a formulation for used a feed,

comprising active XOR in combination with one or more electron donors and/or one or more electron acceptors;

(3) a method of making a formulation for use as a feed, comprising adding a composition comprising active XOR; and

(4) a method of feeding an infant with formula feed, which includes active XOR.

ACTIVITY - Bactericidal.

MECHANISM OF ACTION - XOR is actually a mixture of oxidase and reductase. In presence of oxygen, XOR can generate hydrogen peroxide and superoxide, both bactericidal; under hypoxic conditions as may be found in the gastrointestinal system at weakly acidic pH, inorganic **nitrite** and **nitrate** are reduced to **nitric oxide** (NO), also with some bactericidal activity, but which interacts with superoxide to form peroxynitrite, a potent bactericidal species.

USE - XOR is of use in or added to formula feeds, to reduce the risk of gastrointestinal (GI) infection by pathogenic bacteria (claimed). In humans, this applies particularly for babies and adults who require enteral (tube or sip) feeding. Other animals, notably baby animals, usually calves and piglets, taken from their mothers after birth and fed on waste milk or prior art formula feed, also benefit, with reduced risk of scours disease, dehydration, and death from GI infections. (claimed).

ADVANTAGE - XOR enzyme is not present in normal formula and enteral feeds, and is either absent, or inactivated in heat treatments in the production process. Studies have shown that babies fed prior art formula feeds are about 20 times more likely to suffer from GI infections than those on breast milk.

DESCRIPTION OF DRAWING(S) - The drawing shows the effect of xanthine oxidase in conjunction with NADH and NaNO2, to provide NO generation, on the viability of Escherichia coli in the presence of varying concentrations of oxygen.

Dwg.3/8

TECH UPTX: 20000426

TECHNOLOGY FOCUS - FOOD - Preferred Components: The XOR formulations include buttermilk, a good source of XOR, unless the subject is allergic to buttermilk. The XOR is present in the range 50-150micro-g/ml, exceeding the normal physiological concentration. Electron donors and/or acceptors are also optionally added to aid redox reactions.

Preferred Product: The formulation may be either liquid, or in the form of a powder. Both one and **two** component systems, in **two containers**, are visualized, the latter allows standard heat treatment of one component, with the XOR in the other, to be added at time of use. XOR is, of course, inactivated at high processing temperatures, although pasteurization is allowable. Alternatively, the XOR may be added by the manufacturer to the high temperature treated feed composition. The second portion of the combination has been heat treated, and the first portion has been pasteurized.

Preferred method: The method of preparing the feed formulation, comprises preparing a first portion of the formulation, comprising a composition including active XOR, preparing a second portion, and mixing the two portions to form the formulation. The first portion comprises lyophilized buttermilk and the second portion is a treated feed composition.

L3 ANSWER 9 OF 9 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1970-11703R [08] WPIDS
TI Treating gas containing nitrogen peroxide.
DC J01
PA (MITS) MITSUBISHI JUKOGYO KK AND
CYC 4
PI FR 1578561 A (197008)*
GB 1241576 A (197130)
JP 47010843 B (197214)
CA 926590 A (197323)

PRAI JP 1967-54338 19670824
AB FR 1578561 A UPAB: 19930831

Nitric oxide in waste furnace gases is eliminated by subjecting a **separated part** of the gas to oxidation to convert the NO to nitrogen peroxide, NO2, and then mixing this oxidised portion with the remainder of the gas, the proportion being such that the NO and NO2 are now in equimolecular properties or the NO2 is in excess excess and contacting the mixture with an absorbing alkaline solution, which absorbs the oxides in the form of **nitrite**. The alkaline solution containing white is treated with acid to release NO2 which is then mixed with more of the original NO-containing gas to produce at least equimolecular proportions followed by further alkaline absorption as before.

An apparatus may be used with a number of separate successive treatment zones.

L7 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:717259 CAPLUS
DN 141:392274
TI Local action of exogenous nitric oxide (NO) on the skin blood flow of rock pigeons (Columba livia) is affected by acclimation and skin site
AU Peltonen, Liisa M.; Pyoernilae, Ahti
CS Department of Basic Veterinary Sciences, Physiology, 00014 University of Helsinki, Helsinki, FIN 00014, Finland
SO Journal of Experimental Biology (2004), 207(15), 2611-2619
CODEN: JEBIAM; ISSN: 0022-0949
PB Company of Biologists Ltd.
DT Journal
LA English
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB The authors studied the blood flow over dorsal and abdominal, non-brooding patch skin of two groups of pigeons: one group was thermally acclimated to cold (winter-acclimatized, WAC) while the other group was acclimated to a mesic environment (thermally non-challenged, NOC). Two bilateral patches at the measurement sites were treated simultaneously with a **gel** contg. sodium **nitrate** and ascorbic acid, to generate **nitric oxide** (NO), and a vehicle **gel**. Blood flow was measured by laser Doppler velocimetry. Changes induced by these treatments were calcd. against basic blood flow values for the corresponding patch. The results showed that the basic blood flow over the abdominal skin patches at room temp. was higher than over the dorsal skin in both acclimation states, but comparison revealed a sustainably higher level of basic skin blood flow in the WAC pigeons. The local response to exogenous NO was non-uniform over the two skin areas measured, and a specific vasodilatory action on the abdominal microvessels was recorded in the NOC pigeons. Abdominal vasodilatation in the WAC pigeons seemed to involve other mechanisms as well as local NO-dependent ones, among which the role of cold-induced vasodilatation (CIVD) is discussed here. Interestingly, the dorsal skin seemed to be less responsive to the action of NO, irresp. of the acclimation state. The authors' results show that acclimation state and skin site affect the action of exogenous NO on local skin blood flow, and the authors suggest that the differences reflect acclimation-induced changes in the vascularity of the skin and in its sensitivity to thermal stimuli and that the roles of the abdominal and dorsal skin are different with respect to environmental changes.

L7 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:34564 CAPLUS
DN 140:125852
TI Nitrite in saliva increases gastric mucosal blood flow and mucus thickness
AU Bjoerne, Hakan; Petersson, Joel; Phillipson, Mia; Weitzberg, Eddie; Holm, Lena; Lundberg, Jon O.
CS Department of Anesthesiology and Intensive Care, Karolinska Hospital, Stockholm, Swed.
SO Journal of Clinical Investigation (2004), 113(1), 106-114
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal
LA English
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Salivary nitrate from dietary or endogenous sources is reduced to nitrite by oral bacteria. In the acidic stomach, nitrite is further reduced to NO and related compds., which have potential biol. activity. We used an in vivo rat model as a bioassay to test effects of human saliva on gastric mucosal blood flow and mucus thickness. Gastric mucosal blood flow and

mucus thickness were measured after topical administration of human saliva in HCl. The saliva was collected either after fasting (low in nitrite) or after ingestion of sodium nitrate (high in nitrite). In addnl. expts., saliva was exchanged for sodium nitrite at different doses. Mucosal blood flow was increased after luminal application of nitrite-rich saliva, whereas fasting saliva had no effects. Also, mucus thickness increased in response to nitrite-rich saliva. The effects of **nitrite**-rich saliva were similar to those of **topically** applied sodium **nitrite**. Nitrite-mediated effects were assocd. with generation of NO and S-nitrosothiols. In addn., pretreatment with an inhibitor of guanylyl cyclase markedly inhibited nitrite-mediated effects on blood flow. We conclude that nitrite-contg. human saliva given luminally increases gastric mucosal blood flow and mucus thickness in the rat. These effects are likely mediated through nonenzymic generation of NO via activation of guanylyl cyclase. This supports a gastroprotective role of salivary nitrate/nitrite.

ST saliva nitrite gastric mucosa blood flow mucus thickness; gastric mucosa circulation **nitrite** saliva guanylyl cyclase **nitric oxide**

IT Thiols (organic), biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(S-nitroso, **nitrite** in relation to; **nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT Circulation
(blood flow; **nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT Stomach
(mucosa; **nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT Diet
Mucus
Saliva
(**nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT Human
(saliva from; **nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT 14797-55-8, **Nitrate**, biological studies
RL: BSU (Biological study, unclassified); FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(**nitrite** derived from; **nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

IT 9054-75-5, Guanylyl cyclase 10102-43-9, **Nitric oxide**, biological studies 14797-65-0, **Nitrite**, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**nitrite** in saliva increases gastric mucosal blood flow and mucus thickness possibly mediated by generation of **nitric oxide** via activation of guanylyl cyclase)

L7 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:729386 CAPLUS
DN 140:299682
TI Electrocatalytic oxidation of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes

AU Liang, Ru-ping; Qiu, Jian-ding; Zou, Xiao-yong; Cai, Pei-xiang; Mo, Jin-yuan
CS School of Chemistry and Chemical Engineering, Zhongshan University, Canton, 510275, Peop. Rep. China
SO Fenxi Shiyanshi (2003), 22(4), 4-7
CODEN: FENSE4; ISSN: 1000-0720
PB Fenxi Shiyanshi Bianjibu
DT Journal
LA Chinese
TI Electrocatalytic oxidation of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes
ST electrocatalytic oxidn **nitric oxide** sol **gel** cobalt Phen electrode
IT Sol-**gel** processing
(coating; electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT Blood serum
Cyclic voltammetry
Oxidation, electrochemical
(electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT Electrodes
(glassy carbon, sol-**gel**-Co (Phen)2 modified; electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT Coating process
(sol-**gel**; electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT 10102-43-9, **Nitric oxide**, analysis
RL: ANT (Analyte); ANST (Analytical study)
(electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT 50-81-7, Ascorbic acid, analysis 51-61-6, Dopamine, analysis 74-79-3, L-Arginine, analysis 14797-65-0, **Nitrite**, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT 7440-48-4, Cobalt, uses 77656-97-4, PHEN
RL: DEV (Device component use); USES (Uses)
(electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)
IT 7631-86-9, Silica, uses
RL: NUU (Other use, unclassified); USES (Uses)
(electrocatalytic oxidn. of **nitric oxide** at sol-**gel**-Co(Phen)2 modified electrodes)

L7 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:721715 CAPLUS
DN 140:159704
TI Nitric oxide appears to be a mediator of solar-simulated ultraviolet radiation-induced immunosuppression in humans
AU Kuchel, Johanna M.; Barnetson, Ross St. C.; Halliday, Gary M.
CS Department of Medicine (Dermatology), The Melanoma and Skin Cancer Research Institute, Royal Prince Alfred Hospital at The University of Sydney, Sydney, Australia
SO Journal of Investigative Dermatology (2003), 121(3), 587-593
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell Publishing, Inc.
DT Journal
LA English
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB **Topical** application of NG-methyl-L-arginine and 2,2'-dipyridyl were used to examine the resp. roles of **nitric oxide** and reactive oxygen species in solar-simulated UV radiation-induced immunosuppression in humans in vivo. Immunosuppression was studied using a nickel contact hypersensitivity recall model. UV radiation dose-responses were generated to det. the extent to which NG-methyl-L-arginine and 2,2'-dipyridyl affected the immune response. NG-methyl-L-arginine but not 2,2'-dipyridyl protected the immune system from UV radiation-induced suppression. Both NG-methyl-L-arginine and 2,2'-dipyridyl inhibited nitrite prodn. **Nitrite** is a degrdn. product of peroxynitrite, a cytotoxic mediator resulting from reactions between **nitric oxide** and reactive oxygen species. This suggests that nitric oxide, not its downstream product peroxynitrite, was likely to be responsible for solar-simulated UV radiation-induced immunosuppression. In contrast, both nitric oxide and reactive oxygen species were mediators of solar-simulated UV radiation-induced apoptosis and loss of dendritic S-100+ cells (probably Langerhans cells) from the epidermis. It is likely that different mechanisms are involved in these UV-induced endpoints and that events in addn. to Langerhans cell depletion are important for local immune suppression to recall antigens in humans. Understanding the mechanisms of cutaneous UV-induced oxidative stress will assist in the future design of novel products that protect skin from photoaging and skin cancer.

L7 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:133007 CAPLUS
DN 138:163505
TI Treatment of nail infections with NO
IN Benjamin, Nigel
PA Aberdeen University, UK
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003013489	A1	20030220	WO 2002-GB3575	20020802
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1411908	A1	20040428	EP 2002-747613	20020802
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	BR 2002011390	A	20040817	BR 2002-11390	20020802
	JP 2005501069	T2	20050113	JP 2003-518499	20020802
PRAI	GB 2001-19011	A	20010803		
	WO 2002-GB3575	W	20020802		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Drug delivery systems
(aq.; treatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide**

penetration of nail)

IT Nail (anatomical)
(disease, subungual infection; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(excipients; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(**gels**; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(lacquers; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(liqs.; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(**lotions**; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Alkali metal salts
Alkaline earth salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nitrites**; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(ointments, **creams**; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems
(ointments; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Nail (anatomical), disease
(onychomycosis; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(org.; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Drug delivery systems

(paints; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT Aspergillus niger
Fungicides
Human
Trichophyton rubrum
(treatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT **Nitrites**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT 9003-01-4D, crosslinked
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Carbopol, excipient; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT 9004-32-4, Carboxymethylcellulose 9004-67-5, Methylcellulose 26589-39-9, Eudragits 37353-59-6, Hydroxymethylcellulose
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(excipient; treatment of nail infections with **nitric oxide**-generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT 10102-43-9, Nitrogen oxide (NO), biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT 50-21-5, Lactic acid, biological studies 50-81-7, Ascorbic acid, biological studies 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 65-85-0, Benzoic acid, biological studies 69-72-7, Salicylic acid, biological studies 77-92-9, Citric acid, biological studies 110-16-7, Maleic acid, biological studies 137-66-6, Ascorbyl palmitate 6915-15-7, Malic acid 7632-00-0, Sodium **nitrite** 7758-09-0, Potassium **nitrite** 13465-94-6, Barium **nitrite** 15070-34-5, Magnesium **nitrite**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

IT 526-83-0, Tartaric acid 7782-77-6D, Nitrous acid, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.tau.reatment of nail infections with **nitric oxide** -generating compns. comprising an org. acid and a **nitrite** in relation to formulation and **nitric oxide** penetration of nail)

L7 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:298192 CAPLUS
DN 137:97670
TI Selective reduction of nitrogen monoxide with propene over Ga2O3-Al2O3: Structural characterization and reaction mechanistic study
AU Haneda, Masaaki; Kintaichi, Yoshiaki; Hamada, Hideaki
CS National Institute of Advanced Industrial Science and Technology, AIST Tsukuba Central 5, Ibaraki, 305-8565, Japan
SO Recent Research Developments in Physical Chemistry (2001), 5(Pt. 1), 15-36
CODEN: RRPCFK
PB Transworld Research Network
DT Journal; General Review
LA English
RE.CNT 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Reduction catalysts
(gallium oxide-alumina; sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT Exhaust gases (engine)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT **Nitrates**, processes
Nitrites
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); FORM (Formation, nonpreparative); PROC (Process)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT 115-07-1, Propene, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reductant; sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT 1344-28-1, Alumina, uses 12024-21-4, Gallium oxide
RL: CAT (Catalyst use); PRP (Properties); USES (Uses)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT 7727-37-9, Nitrogen, processes
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); FORM (Formation, nonpreparative); PROC (Process)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)
IT 10102-43-9, **Nitric oxide**, processes 10102-44-0, Nitrogen dioxide, processes
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); POL (Pollutant); REM (Removal or disposal); OCCU (Occurrence); PROC (Process)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)

IT 7782-44-7, Oxygen, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(sol-**gel** vs. impregnated catalyst prepn. effect on and proposed reaction mechanism for selective redn. of exhaust gas **nitric oxide** by propene over gallium-alumina catalyst)

L7 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:171653 CAPLUS
DN 136:205458
TI Transdermal pharmaceutical delivery system
IN Tucker, Arthur Tudor; Benjamin, Nigel
PA Queen Mary & Westfield College, UK
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002017881	A2	20020307	WO 2001-GB3863	20010830
	WO 2002017881	A3	20030417		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001084191	A5	20020313	AU 2001-84191	20010830
	EP 1328252	A2	20030723	EP 2001-963158	20010830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004507486	T2	20040311	JP 2002-522855	20010830
	US 2004013747	A1	20040122	US 2003-363439	20030616
PRAI	GB 2000-21317	A	20000830		
	WO 2001-GB3863	W	20010830		

AB A pharmaceutically delivery system is described comprising a drug and acidified **nitrite** as an agent to produce local prodn. of **nitric oxide** at the skin surface. The dosage form may be in any acceptable carrier and comprises an acidifying agent adapted to reduce the pH at the environment. In one embodiment, a barrier consisting of a membrane allows diffusions of the anesthetic and nitrite ions, while preventing direct contact of the skin and acidifying agent. A **nitric oxide**-generating **gel** (NO-generating **gel**) was prepd. as follows. Sodium nitrite was added to KY JellyTM to make a 5% soln. and ascorbic acid was also added to KY JellyTM to make a 5% soln. Approx. 0.5 mL each soln. was mixed together on the skin of a patient by using a sterile swab. The microcirculatory response to topical application of a NO-generating gel was measured in 10 healthy subjects. The vasodilator response to the active treatment reached a plateau phase in all patients within the 10 min of active gel application. Forearm skin and finger pulp blood flow increased markedly following topical application of a NO-generating gel in the healthy volunteers. When the active gel was applied to the forearm skin all subjects showed a large vasodilator response to active gel treatment in both vol. and flux.

L7 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:142594 CAPLUS

DN 136:161405
TI Compositions including ammonia oxidizing bacteria to increase production of nitric oxide and nitric oxide precursors and methods of using same
IN Whitlock, David R.
PA USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002013982	A1	20020221	WO 2001-US25248	20010810
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2414941	AA	20020221	CA 2001-2414941	20010810
	AU 2001084849	A5	20020225	AU 2001-84849	20010810
	EP 1313574	A1	20030528	EP 2001-963935	20010810
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013085	A	20030722	BR 2001-13085	20010810
	JP 2004506028	T2	20040226	JP 2002-519111	20010810
	US 2004014188	A1	20040122	US 2003-332933	20030114
	ZA 2003000377	A	20040122	ZA 2003-377	20030114
PRAI	US 2000-224598P	P	20000811		
	WO 2001-US25248	W	20010810		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Cosmetics
(**creams**; compns. including ammonia oxidizing bacteria to increase prodn. of **nitric oxide** and **nitric oxide** precursors for enhancement of health)
IT Drug delivery systems
(ointments, **creams**; compns. including ammonia oxidizing bacteria to increase prodn. of **nitric oxide** and **nitric oxide** precursors for enhancement of health)
IT Drug delivery systems
(**topical**; compns. including ammonia oxidizing bacteria to increase prodn. of **nitric oxide** and **nitric oxide** precursors for enhancement of health)
IT 50-21-5, Lactic acid, biological studies 7439-89-6D, Iron, salts 7647-14-5, Sodium chloride, biological studies 14797-55-8, **Nitrate**, biological studies 14797-65-0, **Nitrite**, biological studies
RL: BUU (Biological use, unclassified); COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. including ammonia oxidizing bacteria to increase prodn. of **nitric oxide** and **nitric oxide** precursors for enhancement of health)

L7 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:868945 CAPLUS
DN 136:575
TI Infrared thermography and methods of use
IN Marek, Przemyslaw A.; Trocha, Andzrej M.

PA Nitromed, Inc., USA
SO U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001046471	A1	20011129	US 2001-850081	20010508
	US 6762202	B2	20040713		
	US 2004162243	A1	20040819	US 2004-781705	20040220
PRAI	US 2000-202935P	P	20000509		
	US 2001-850081	A1	20010508		

OS MARPAT 136:575
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Drug delivery systems
(**gels**; IR thermog. for measuring vasodilation or changes in blood flow following administration of **nitric oxide** donor)
IT Drug delivery systems
(**lotions**; IR thermog. for measuring vasodilation or changes in blood flow following administration of **nitric oxide** donor)
IT Drug delivery systems
(ointments, **creams**; IR thermog. for measuring vasodilation or changes in blood flow following administration of **nitric oxide** donor)
IT Drug delivery systems
(**topical**; IR thermog. for measuring vasodilation or changes in blood flow following administration of **nitric oxide** donor)
IT 542-56-3, Isobutyl **nitrite**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IR thermog. for measuring vasodilation or changes in blood flow following administration of **nitric oxide** donor)

L7 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:703043 CAPLUS
DN 135:251985
TI Compositions and kits comprising .alpha.-adrenergic receptor antagonists and nitric oxide donors and methods of use in the treatment of impotence
IN Garvey, David S.; Schroeder, Joseph D.; Saenz de Tejada, Inigo
PA NitroMed, Inc., USA
SO U.S., 37 pp., Cont.-in-part of U.S. 5,994,294.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6294517	B1	20010925	US 1998-145143	19980901
	US 5932538	A	19990803	US 1996-595732	19960202
	US 5994294	A	19991130	US 1996-714313	19960918
	WO 9727749	A1	19970807	WO 1997-US1294	19970128
	W: AU, CA, IL, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6514934	B1	20030204	US 1999-280540	19990330
	US 6323211	B1	20011127	US 1999-285048	19990402
	US 6417162	B1	20020709	US 1999-306809	19990507

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     US 6433182           B1    20020813    US 1999-306805          19990507
     CA 2339145           AA    20000309    CA 1999-2339145         19990901
     WO 2000012075        A1    20000309    WO 1999-US20023         19990901
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
             MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
             SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9957016           A1    20000321    AU 1999-57016           19990901
     AU 770414            B2    20040219
     EP 1109542           A1    20010627    EP 1999-944040          19990901
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002523449        T2    20020730    JP 2000-567193          19990901
     US 6469065           B1    20021022    US 1999-387724          19990901
     US 2002143007        A1    20021003    US 2002-146671          20020516
PRAI US 1996-595732       A2    19960202
     US 1996-714313       A2    19960918
     WO 1997-US1294       A2    19970128
     US 1998-145143       A3    19980901
     WO 1999-US20023      W     19990901
OS   MARPAT 135:251985
RE.CNT  60    THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT   Drug delivery systems
        (topical; .alpha.-adrenergic receptor antagonists and
        nitric oxide donors for treatment of impotence)
IT   54-32-0   70-18-8, reactions   75-36-5, Acetyl chloride   108-55-4,
     Glutaric anhydride   540-80-7, tert-Butyl nitrite   7632-00-0,
     Sodium nitrite   19216-56-9   24424-99-5, Di-tert-
     butyldicarbonate   25512-65-6, Dihydropyran   40077-13-2   57149-07-2
     59729-24-7   61040-78-6, 2,4,6-Trimethoxybenzyl alcohol   87261-63-0
     361520-75-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction; .alpha.-adrenergic receptor antagonists and nitric
        oxide donors for treatment of impotence)

L7   ANSWER 11 OF 43  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2001:635927  CAPLUS
DN   135:190432
TI   Methods and compositions for improving sleep based on nitric oxide
     mimetics
IN   Ackman, C. Bruce; Adams, Michael A.; Heaton, Jeremy P. W.; Ratz, Jordan D.
PA   Vaxis Therapeutics Corporation, Can.
SO   PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2001062290         A2    20010830    WO 2001-CA207           20010222
     WO 2001062290         A3    20020801
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
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YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA	2400708	AA	20010830	CA 2001-2400708	20010222
US	2002015740	A1	20020207	US 2001-791127	20010222
US	6586478	B2	20030701		
EP	1267862	A2	20030102	EP 2001-907282	20010222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP	2003523405	T2	20030805	JP 2001-561354	20010222
US	2003195140	A1	20031016	US 2003-387269	20030311
PRAI US	2000-184087P	P	20000222		
US	2000-236727P	P	20001002		
US	2001-791127	A3	20010222		
WO	2001-CA207	W	20010222		

ST **nitric oxide** mimetic oral **topical** sleep disorder; hypnotic nitric oxide mimetic sleep disorder; nitroglycerin transdermal sleep disorder

IT Drug delivery systems
(**topical**; compns. for improving sleep based on **nitric oxide** mimetics)

IT 55-63-0, Nitroglycerin 14402-89-2, Sodium nitroprusside 16051-77-7, Isosorbide 5-**nitrate** 25717-80-0, Molsidomine 65141-46-0, Nicorandil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for improving sleep based on **nitric oxide** mimetics)

L7 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:369237 CAPLUS
DN 136:107360
TI A novel method for the delivery of nitric oxide therapy to the skin of human subjects using a semi-permeable membrane
AU Hardwick, J. B. J.; Tucker, A. T.; Wilks, M.; Johnston, A.; Benjamin, N.
CS Department of Clinical Pharmacology, St. Bartholomew's and the Royal London School of Medicine and Dentistry, London, EC1M 6BQ, UK
SO Clinical Science (2001), 100(4), 395-400
CODEN: CSCIAE; ISSN: 0143-5221
PB Portland Press Ltd.
DT Journal
LA English
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ST **nitric oxide** Sympatex **topical** delivery antimicrobial

IT Drug delivery systems
(**topical**; delivery of **nitric oxide** therapy to skin of human subjects using a semi-permeable membrane)

IT 50-81-7, Ascorbic acid, reactions 7632-00-0, Sodium **nitrite**
RL: RCT (Reactant); RACT (Reactant or reagent)
(delivery of **nitric oxide** therapy to skin of human subjects using a semi-permeable membrane)

L7 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:116408 CAPLUS
DN 135:147363
TI **Topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure
AU Lysy, J.; Israelit-Yatzkan, Y.; Sestiery-Ittah, M.; Weksler-Zangen, S.;

Keret, D.; Goldin, E.
CS Department of Gastroenterology, Hadassah University Hospital, Jerusalem, Israel
SO Gut (2001), 48(2), 221-224
CODEN: GUTTAK; ISSN: 0017-5749
PB BMJ Publishing Group
DT Journal
LA English
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI **Topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure
AB Anal fissure is perpetuated by high sphincter pressures and secondary local ischemia. Pharmacol. approaches include **topical nitrates** and botulinum toxin (BT) which act to reduce anal pressure. BT lowers anal pressure by preventing acetylcholine release from nerve terminals while **topical nitrates** act by donating **nitric oxide** (NO). The aims of the present study were to compare the therapeutic effect and lowering action on internal anal sphincter pressure of BT injection and local application of isosorbide dinitrate (ID) compared with BT given alone, in patients with chronic anal fissure (CAF) refractory to treatment with ID. Thirty consecutive patients with CAF who did not respond to previous topical ID treatments were randomly assigned to receive one of the following treatments: group A, injection of BT (20 U into the internal anal sphincter) and subsequent daily applications of ID (2.5 mg three times daily for three months); and group B, BT injection only (20 U). If at the end of six weeks following BT injection no improvement was seen in group B, ID was added. A series of anal pressure measurements, including resting basal pressure and resting pressure following topical ID (1.25, 2.5, and 3.75 mg), was carried out both before and two weeks after 20 U of BT injection into the internal anal sphincter. At the end of the trial, patients were followed up for an av. period of 10 mo. At six weeks the fissure healing rate was significantly higher in group A patients (10/15 (66%)) compared with group B (3/15 (20%)) ($p=0.025$). At eight and 12 wk, no significant differences were seen: 11/15 (73%) v 11/15 (73%) and 9/15 (60%) v 10/15 (66%), group A v group B, resp. Maximum anal resting pressure (MARP) was significantly lower two weeks after BT injection than baseline MARP (90 (4) v 110 (5) mm Hg; $p<0.001$). A significantly greater redn. in MARP following local application of ID was achieved after BT injection compared with that achieved before BT injection ($p=0.037$). (1) Combined BT injection and local application of ID in patients with CAF who failed previous treatment with ID was more effective than BT alone. This treatment modality appears to be safe and promising. (2) ID application induced a greater redn. in MARP following BT injection compared with ID application before BT injection. The improved potency of ID on MARP after BT injection suggests a primary cholinergic tonus dominance in some patients and not, as previously claimed, anal sphincter insensitivity to nitrates.
IT Intestine
(internal anal sphincter; **topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure)
IT **Nitrates**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure)
IT 107231-12-9, Botulin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure)

IT 51-84-3, Acetylcholine, biological studies 10102-43-9, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**topical nitrates** potentiate the effect of botulinum toxin in the treatment of patients with refractory anal fissure)

L7 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:645862 CAPLUS
DN 133:227834
TI Pharmaceutical composition containing nitrate source and an acidifying agent for treating skin ischemia
IN Tucker, Arthur Tudor; Benjamin, Nigel
PA Queen Mary & Westfield College, UK
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053193	A1	20000914	WO 2000-GB853	20000309
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1161248	A1	20011212	EP 2000-907851	20000309
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002538210	T2	20021112	JP 2000-603682	20000309
	US 2002090401	A1	20020711	US 2001-949202	20010907
PRAI	GB 1999-5425	A	19990309		
	WO 2000-GB853	W	20000309		

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The use of acidified **nitrite** as an agent to produce local prodn. of **nitric oxide** at the skin surface is described in the treatment of peripheral ischemia and assocd. conditions. The dosage form may be in any pharmaceutically acceptable carrier means and comprises an acidifying agent adapted to reduce the pH at the environment. A barrier consisting of a membrane allows diffusions of the nitrite ions while preventing direct contact of the skin and acidifying agent. Among the many potential applications for the invention is the management of chronic skin wounds, peripheral ischemia conditions such as Raynaud's phenomenon. The microcirculatory response to **topical** application of a compn. contg. Na **nitrite** and ascorbic acid in KY Jelly was detd.

ST skin ischemia **nitrate** acid **topical**

IT Drug delivery systems
(**topical**; pharmaceutical compn. contg. **nitrate** source and an acidifying agent for treating skin ischemia)

IT 10102-43-9, **Nitric oxide**, biological studies
14797-65-0, Nitrite, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(pharmaceutical compn. contg. **nitrate** source and an acidifying agent for treating skin ischemia)

L7 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:559203 CAPLUS
DN 133:344208
TI A **topical nitric oxide**-generating therapy for cutaneous leishmaniasis
AU Davidson, Robert N.; Yardley, Vanessa; Croft, Simon L.; Konecny, Pamela; Benjamin, Nigel
CS Department of Infection and Tropical Medicine, Northwick Park Hospital, Harrow, UK
SO Transactions of the Royal Society of Tropical Medicine and Hygiene (2000), 94(3), 319-322
CODEN: TRSTAZ; ISSN: 0035-9203
PB Royal Society of Tropical Medicine and Hygiene
DT Journal
LA English
RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI A **topical nitric oxide**-generating therapy for cutaneous leishmaniasis
ST **nitric oxide** leishmanicide ascorbate salicylate **nitrate**; ointment nitric oxide leishmanicide
IT Protozoacides
(leishmanicides; **topical nitric oxide**-generating therapy for cutaneous leishmaniasis)
IT Drug delivery systems
(ointments, **creams**; **topical nitric oxide**-generating therapy for cutaneous leishmaniasis)
IT Leishmania major
Leishmania tropica
(**topical nitric oxide**-generating therapy for cutaneous leishmaniasis)
IT 69-72-7, Salicylic acid, biological studies 7758-09-0, Potassium **nitrite** 10102-43-9, **Nitric oxide**, biological studies 62624-30-0, Ascorbic acid
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**topical nitric oxide**-generating therapy for cutaneous leishmaniasis)

L7 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:92763 CAPLUS
DN 132:117156
TI Molluscum contagiosum effectively treated with a **topical** acidified **nitrite**, **nitric oxide** liberating **cream**
AU Ormerod, A. D.; White, M. I.; Shah, S. A. A.; Benjamin, N.
CS Aberdeen Royal Infirmary, Department of Dermatology, Aberdeen, AB25 2ZN, UK
SO British Journal of Dermatology (1999), 141(6), 1051-1053
CODEN: BJDEAZ; ISSN: 0007-0963
PB Blackwell Science Ltd.
DT Journal

LA English
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI Molluscum contagiosum effectively treated with a **topical** acidified **nitrite, nitric oxide** liberating **cream**
AB A double-blind, group-sequential clin. trial of acidified **nitrite** was performed to demonstrate the efficacy of this **nitric oxide** donor in treating molluscum contagiosum. Subjects received either 5% sodium **nitrite** co-applied with 5% salicylic acid under occlusion, or identical **cream** with v salicylic acid, omitting sodium **nitrite**. Active and control treatment groups were well matched for the no. and duration of lesions and made a similar no. of applications. We found a 75% cure rate in the active treatment group and 21% cure with control treatment (P = 0.cntdot.01). The mean time to cure was 1.cntdot.83 mo. Staining of the skin and irritation were frequent side-effects but did not prevent successful treatment.
ST **nitrite cream** antiviral molluscum contagiosum virus; antiviral nitrite molluscum contagiosum virus
IT Antiviral agents
Molluscum contagiosum virus
(molluscum contagiosum effectively treated with a **topical** acidified **nitrite, nitric oxide** liberating **cream** in humans)
IT Drug delivery systems
(ointments, **creams**; molluscum contagiosum effectively treated with a **topical** acidified **nitrite, nitric oxide** liberating **cream** in humans)
IT 14797-65-0, **Nitrite**, biological studies
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(molluscum contagiosum effectively treated with a **topical** acidified **nitrite, nitric oxide** liberating **cream** in humans)
IT 10102-43-9, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(molluscum contagiosum effectively treated with a **topical** acidified **nitrite, nitric oxide** liberating **cream** in humans)

L7 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:798594 CAPLUS
DN 132:30578
TI Effect of nitric-oxide-generating system on microcirculatory blood flow in skin of patients with severe Raynaud's syndrome: a randomized trial
AU Tucker, A. T.; Pearson, R. M.; Cooke, E. D.; Benjamin, N.
CS Clinical Microvascular Unit, St Bartholomew's Hospital, London, UK
SO Lancet (1999), 354(9191), 1670-1675
CODEN: LANCAO; ISSN: 0140-6736
PB Lancet Ltd.
DT Journal
LA English
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Patients with Raynaud's syndrome have abnormal digital vasoconstriction, which may be secondary to impaired synthesis of, or impaired sensitivity to, nitric oxide. We studied the effect on microcirculation of a **nitric-oxide**-generating system applied **topically** to the finger and forearm of healthy volunteers and patients with primary Raynaud's syndrome. We did a single-blind, randomized,

placebo-controlled, cross-over study of the microcirculatory response to **topical** application of a **nitric-oxide** -generating **gel** in 20 patients with severe Raynaud's syndrome, and ten healthy volunteers. We prepd. the **nitric-oxide** -generating system by mixing a soln. of KY jelly and sodium **nitrite** (5% wt./vol.), with a soln. of KY jelly and ascorbic acid (5% wt./vol.). About 0.5 mL of each soln. was sep. applied to the skin of the forearm (3 cm2), and then mixed with a sterile cotton bud. A similar procedure was done simultaneously on the other arm with KY jelly only (placebo). The procedure was then repeated on the finger pulps. Changes in skin microcirculatory vol. and flux were measured bilaterally by IR photoplethysmog. and laser doppler fluxmetry, resp. In the forearm, blood flow increased significantly after application of the active gel both in patients with Raynaud's syndrome (microcirculatory vol. from mean area under the curve 98 [SE 14] to 1024 [130]; microcirculatory flux from 5060 [462] to 74800 [3940]) and in healthy controls (vol. from 85 [19] to 1020 [60]; flux from 4420 [435] to 84500 [7000]). In the fingers, although baseline blood flow was lower in patients than in controls, both groups showed increases with application of active gel (vol. from 1100 [194] to 3280 [672] and 2380 [441] to 6160 [1160], resp.; flux from 33 400 [4200] to 108 000 [13 600] and 52 000 [8950] to 185 000 [19 500]). Increases in blood flow with placebo gel were not significant. No adverse effects were reported. In primary Raynaud's syndrome, **topical** application of a **nitric-oxide**-generating system can stimulate an increase in both microcirculatory vol. and flux.

L7 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:592370 CAPLUS
DN 131:317723
TI The inflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin
AU Ormerod, Anthony David; Copeland, Paul; Hay, Isabelle; Husain, Akhtar; Ewen, Stanley W. B.
CS Department of Dermatology, Aberdeen Royal Infirmary, Aberdeen, AB25 2ZN, UK
SO Journal of Investigative Dermatology (1999), 113(3), 392-397
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell Science, Inc.
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The inflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin
AB We describe the pro-inflammatory and cytotoxic effects of nitric oxide in vivo in human skin. **Nitrite** and ascorbic acid were mixed on the skin of 12 normal volunteers, three times daily, to release **nitric oxide**. Exposure to **nitric oxide** was varied by randomizing the concn. of **nitrite** and duration of application. Nitric oxide treated skin showed significant increases in cells expressing CD3, CD4, CD8, CD68, neutrophil elastase, ICAM-1, VCAM-1, nitrosotyrosine, p53, and apoptotic cells compared with skin treated with ascorbic acid alone. There was no significant increase in mast cells. Following application of nitric oxide there were significantly fewer CD1a pos. Langerhans cells in the epidermis. These appeared to lose dendritic morphol. and migrate from the epidermis. There was no significant difference in staining for Ki-67, a marker related to proliferating cell nuclear antigen, between active and control skin but staining was greater after exposure to higher dose nitric oxide than the low dose. Apoptosis, cytotoxicity, and p53 staining were relatively greater after 48 h exposure than after 24 h. These results suggest that nitric oxide is proinflammatory and is toxic to DNA, leading to the accumulation of p53

and subsequent apoptosis. High-dose nitric oxide paradoxically led to a smaller increase in macrophages and T cells than low dose suggesting an immunosuppressive effect of higher levels.

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1); proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT Cell adhesion molecules
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(VCAM-1; proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT Apoptosis
Cytotoxicity
Immunosuppression
Inflammation
Macrophage
Mast cell
Skin
T cell (lymphocyte)
(proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT CD3 (antigen)
CD4 (antigen)
CD68 (antigen)
CD8 (antigen)
p53 (protein)
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT 9004-06-2, Elastase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neutrophil; proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT 50-81-7, L-Ascorbic acid, biological studies 10102-43-9, **Nitric oxide**, biological studies 14797-65-0, **Nitrite**, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

IT 194294-62-7
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proinflammatory and cytotoxic effects of a **nitric oxide** releasing **cream** on normal skin)

L7 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:576795 CAPLUS
DN 131:204625
TI Inorganic **nitrite** and organic acid in combination as **topical** antiviral composition
IN Ormerod, Anthony; Benjamin, Nigel
PA Aberdeen University, UK
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9944622	A1	19990910	WO 1999-GB605	19990301
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2322199	AA	19990910	CA 1999-2322199	19990301
	AU 9932617	A1	19990920	AU 1999-32617	19990301
	AU 758264	B2	20030320		
	BR 9908617	A	20001205	BR 1999-8617	19990301
	EP 1059928	A1	20001220	EP 1999-937878	19990301
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002505295	T2	20020219	JP 2000-534223	19990301
	NZ 506678	A	20030429	NZ 1999-506678	19990301
	NO 2000004302	A	20001030	NO 2000-4302	20000829
	US 2004105898	A1	20040603	US 2003-701295	20031103
PRAI	GB 1998-4469	A	19980302		
	GB 1994-3284	A	19940221		
	GB 1994-4365	A	19940307		
	WO 1995-GB338	A1	19950217		
	US 1996-696930	B2	19960821		
	WO 1999-GB605	W	19990301		
	US 1999-330654	A1	19990611		

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Inorganic **nitrite** and organic acid in combination as **topical** antiviral composition

IT Antiviral agents
Wart
(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT Carboxylic acids, biological studies
Paraffin waxes, biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT **Nitrites**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT Drug delivery systems
(liposomes; inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT Drug delivery systems
(microspheres; inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT Drug delivery systems
(**topical**; inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT 10102-43-9, **Nitric oxide**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)

(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT 7632-00-0, Sodium **nitrite**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

IT 50-21-5, biological studies 50-81-7, L-Ascorbic acid, biological studies 64-18-6, Formic acid, biological studies 65-85-0, Benzoic acid, biological studies 69-72-7, Salicylic acid, biological studies 77-92-9, biological studies 87-69-4, biological studies 137-66-6, Ascorbyl palmitate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg. **nitrite** and org. acid in combination as **topical** antiviral compn.)

L7 ANSWER 20 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:351746 CAPLUS
DN 129:32332
TI Treatment of equine laminitis
IN Russell, Meri Charmyne
PA Mortar & Pestle Veterinary Pharmacy, Inc., USA
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9822090	A1	19980528	WO 1997-US20668	19971117
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5891472	A	19990406	US 1996-752415	19961119
	US 6045827	A	20000404	US 1997-914230	19970819
	CA 2273183	AA	19980528	CA 1997-2273183	19971117
	AU 9854359	A1	19980610	AU 1998-54359	19971117
	EP 946147	A1	19991006	EP 1997-948262	19971117
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001509136	T2	20010710	JP 1998-519798	19971117
	BR 9714573	A	20020723	BR 1997-14573	19971117
	MX 9905262	A	20000630	MX 1999-5262	19990607
	US 6287601	B1	20010911	US 1999-333974	19990616
PRAI	US 1996-752415	A	19961119		
	US 1997-914230	A1	19970819		
	WO 1997-US20668	W	19971117		

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Drug delivery systems
(**gels**; treatment of equine laminitis with **nitric oxide** donors and NSAID)

IT Drug delivery systems
(ointments, **creams**; treatment of equine laminitis with **nitric oxide** donors and NSAID)

IT Drug delivery systems
(**topical**; treatment of equine laminitis with **nitric oxide** donors and NSAID)
IT 55-63-0, Nitroglycerin 74-79-3, L-Arginine, biological studies 288-13-1D, Pyrazole, analogs 7803-49-8, Hydroxylamine, biological studies 14343-69-2, Azide 14797-65-0, **Nitrite**, biological studies 15078-28-1, Nitroprusside 15687-27-1 22071-15-4, Ketoprofen 22204-53-1, Naproxen 39455-90-8D, Pyrazolone, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of equine laminitis with **nitric oxide** donors and NSAID)

L7 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:771990 CAPLUS
DN 128:85741
TI Studies on the structural background on the cross-inhibition of the products in the arginine metabolism of macrophages
AU Hrabak, Andras; Bajor, Tamas; Temesi, Agnes; Meszaros, Gyorgy
CS Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis Medical University, Budapest, H-1444, Hung.
SO Medical Science Monitor (1997), 3(3), 299-304
CODEN: MSMOFR; ISSN: 1234-1010
PB Medical Science International Publishing
DT Journal
LA English
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB Arginase and **nitric oxide** synthase (NOS) were inhibited by **nitrite** and putrescine, resp. Results showed a cross-inhibition by the products of the two arginine utilizing pathways in macrophages. The kinetics of these inhibitions have been described earlier. Arginase was measured by the release of urea; NOS activity was detd. by measuring 14C-L-citrulline synthesis from 14C-labeled L-arginine. The structural changes of arginase were studied by fluorescence and gel filtration expts. **Nitrite** caused a decrease of tryptophane fluorescence over 5 mM concn. without dissocg. the arginase oligomers as indicated by **gel** filtration expts. The differences in the structural features of L-arginine substrate and putrescine inhibitor made the binding of putrescine to the active site of NOS unlikely. In conclusion, our studies suggest that nitrite causes a non-competitive inhibition of arginase based on a conformational change without the dissocn. of the arginase oligomers. For putrescine inhibition we suggest an allosteric mechanism also based on a conformational change.
ST nitrite putrescine inhibition arginase arginine; conformation transition nitric oxide synthase arginase; **nitric oxide** synthase inhibition **nitrite** putrescine

L7 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:475088 CAPLUS
DN 127:113367
TI Drug delivery of nitric oxide
IN Tawashi, Rashad
PA Can.
SO U.S., 7 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI US 5648101 A 19970715 US 1994-338664 19941114
PRAI US 1994-338664 19941114
IT **Nitrites**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(drug delivery of **nitric oxide**)
IT Drug delivery systems
(**lotions**; drug delivery of **nitric oxide**)
IT Drug delivery systems
(ointments, **creams**; drug delivery of **nitric oxide**)
IT 7632-00-0, Sodium **nitrite** 7720-78-7, Ferrous sulfate
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(drug delivery of **nitric oxide**)

L7 ANSWER 23 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:721653 CAPLUS
DN 126:1215
TI Mercapto and seleno derivatives as inhibitors of nitric oxide synthase
IN Southan, Garry J.; Salzman, Andrew L.; Szabo, Csaba
PA Children's Hospital Medical Center, Philadelphia, USA
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9630007	A1	19961003	WO 1996-US3838	19960322
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
	US 5674907	A	19971007	US 1995-410312	19950324
	US 5929063	A	19990727	US 1995-545952	19951020
	AU 9653191	A1	19961016	AU 1996-53191	19960322
	AU 695307	B2	19980813		
	EP 814792	A1	19980107	EP 1996-909808	19960322
	EP 814792	B1	20030528		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11502847	T2	19990309	JP 1996-529506	19960322
	BR 9607951	A	19990601	BR 1996-7951	19960322
	RU 2191575	C2	20021027	RU 1997-116161	19960322
	AT 241347	E	20030615	AT 1996-909808	19960322
PRAI	US 1995-410312	A	19950324		
	US 1995-545952	A	19951020		
	WO 1996-US3838	W	19960322		

OS MARPAT 126:1215
IT Artery
(aorta, smooth muscle cells, **nitrite** formation in; mercapto and seleno derivs. for inhibitors of **nitric oxide** synthase and disease treatment)
IT Macrophage
(**nitrite** formation in; mercapto and seleno derivs. for inhibitors of **nitric oxide** synthase and disease treatment)
IT Drug delivery systems
(**topical**; mercapto and seleno derivs. for inhibitors of

nitric oxide synthase and disease treatment)

IT 14797-65-0, **Nitrite**, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(mercapto and seleno derivs. for inhibitors of **nitric oxide** synthase and disease treatment)

L7 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:587398 CAPLUS
DN 125:271363
TI **Nitric oxide** is generated on the skin surface by reduction of sweat **nitrate**
AU Weller, Richard; Pattullo, Simon; Smith, Lorna; Golden, Michael; Ormerod, Anthony; Benjamin, Nigel
CS Department Dermatology, Aberdeen Royal Hospitals, Aberdeen, UK
SO Journal of Investigative Dermatology (1996), 107(3), 327-331
CODEN: JIDEAE; ISSN: 0022-202X
PB Blackwell
DT Journal
LA English
TI **Nitric oxide** is generated on the skin surface by reduction of sweat **nitrate**
AB Nitric oxide (NO) is known to be synthesized by mammalian cells from L-arginine by a group of NO synthase enzymes. We now show that NO is generated from human skin and propose a different mechanism of prodn. Whereas enzymic NO synthesis is inhibited by monomethyl L-arginine, this arginine analog, when infused into the brachial artery at concns. sufficient to inhibit endothelial NO synthase activity, has little effect on hand skin NO prodn. Hand skin NO prodn. is increased by **topical** acidification of the skin surface and greatly increased by the addn. of **nitrite** solns. We propose that NO generation from skin derives from sweat nitrite (the concn. of which was found to av. 3.4 .mu.M in six subjects) due to chem. redn. consequent to the acidic nature of sweat. Sweat contains nitrate in appreciable amts., and skin commensal bacteria can synthesize nitrate reductase enzyme. Patients on long-term tetracycline antibiotics showed significantly reduced skin NO synthesis, although topical antiseptic and antibiotics had little effect on NO generation in the short-term. We propose that NO generation from skin is dependent on bacterial nitrate redn. to nitrite and subsequent redn. by acidification. We speculate that this has a physiol. role in the inhibition of infection by pathogenic fungi and other susceptible microorganisms and may affect cutaneous T-cell function, keratinocyte differentiation, and skin blood flow.
ST **nitric oxide** sweat **nitrate nitrite** skin
IT Perspiration
Skin
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate**)
IT Microbicidal and microbiostatic action
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate** in relation to)
IT 14797-55-8, **Nitrate**, biological studies 14797-65-0, **Nitrite**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate**)
IT 10102-43-9, **Nitric oxide**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); PROC (Process)
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate**)
IT 60-54-8, Tetracycline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate** in relation to)
IT 12408-02-5, Hydrogen ion, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**nitric oxide** is generated on skin surface by redn. of sweat **nitrate** in relation to)

L7 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:324458 CAPLUS
DN 125:54269
TI Nitric oxide production from human skin
AU Weller, Richard; Patullo, Simon; Smith, Lorna; Golden, Michael; Ormerod, Anthony; Benjamin, Nigel
CS Medical School, University Aberdeen, Foresterhill/Aberdeen, AB9 2ZD, UK
SO Portland Press Proceedings (1996), 10(Biology of Nitric Oxide Part 5), 229
CODEN: POPPEF; ISSN: 0966-4068
PB Portland Press
DT Journal
LA English
AB The mechanism of **nitric oxide** generation from human skin and the importance of generated NO in skin protection from microbial pathogens were studied using inhibitors of NO synthase, **topical** application of antimicrobials, inorg. **nitrite**, and agents altering skin acidity. Changes in hand skin NO generation and forearm blood flow were measured during brachial artery LNMMA infusion. NO prodn. by skin increased during application of pH3 buffer and decreased during the application of pH9 buffer compared to the normal saline control. Potassium nitrite when applied to the hand caused a dose-dependent increase in NO generation which was linear. There was no significant change in hand NO prodn. following chlorhexidine.
ST nitric oxide prodn skin; **nitrite** proton **nitric oxide** prodn skin
IT 12408-02-5, Hydrogen ion, biological studies 14797-65-0, **Nitrite**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**nitric oxide** prodn. from human skin in relation to)

L7 ANSWER 26 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:110381 CAPLUS
DN 124:156005
TI Nitric oxide donor composition and method for treatment of anal disorders
IN Gorfine, Stephen R.
PA Neptune Pharmaceutical Corp., USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9532715	A1	19951207	WO 1995-US4364	19950410
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD,				

MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

	US 5504117	A	19960402	US 1994-250555	19940527
	AU 9522823	A1	19951221	AU 1995-22823	19950410
	EP 719145	A1	19960703	EP 1995-916264	19950410
	EP 719145	B1	20000906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CN 1131392	A	19960918	CN 1995-190687	19950410
	CN 1107499	B	20030507		
	JP 09504037	T2	19970422	JP 1996-500835	19950410
	JP 3211892	B2	20010925		
	AT 196082	E	20000915	AT 1995-916264	19950410
	EP 1051972	A1	20001115	EP 2000-202372	19950410
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	CA 2168247	C	20001212	CA 1995-2168247	19950410
	JP 2001026550	A2	20010130	JP 2000-171337	19950410
	PT 719145	T	20010131	PT 1995-916264	19950410
	ES 2092460	T3	20010201	ES 1995-916264	19950410
	JP 2003073302	A2	20030312	JP 2002-243611	19950410
	IL 113448	A1	20001121	IL 1995-113448	19950420
	US 5693676	A	19971202	US 1996-666264	19960620
	GR 3035001	T3	20010330	GR 2000-402692	20001206
	US 2001025057	A1	20010927	US 2001-812277	20010319
	US 2002161042	A1	20021031	US 2001-21168	20011211
PRAI	US 1994-250555	A	19940527		
	US 1995-371088	A	19950110		
	EP 1995-916264	A3	19950410		
	JP 1996-500835	A3	19950410		
	JP 2000-171337	A3	19950410		
	WO 1995-US4364	W	19950410		
	US 1996-666264	A1	19960620		
	US 1997-970447	A1	19971114		
	US 1999-286251	B1	19990405		

AB A pharmaceutical compn. contains a **nitric oxide** donor and advantageously an optional corticosteroid and/or **topical** anesthetic. The compn. is useful in a method for treating anal disorders such as anal fissure, anal ulcer, hemorrhoidal disease, levator spasm, and so forth, by topical application to or proximate the affected area.

IT Anesthetics
(**topical, nitric oxide** donor compn. contg. corticosteroid and method for treatment of anal disorders)

IT 55-63-0, Nitroglycerin 78-11-5, PentaErythrityl tetranitrate 87-33-2, Isosorbide dinitrate 621-65-8, Glyceryl 1,2-dinitrate 623-87-0, Glyceryl 1,3-dinitrate 624-43-1, Glyceryl 1-mononitrate 628-96-6, Ethylene glycol dinitrate 1712-64-7, Isopropyl **nitrate** 6659-60-5, Butane-1,2,4-triol trinitrate 7297-25-8, Erythrityl tetranitrate 10102-43-9, Nitric oxide, biological studies 16051-77-7, Isosorbide mononitrate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**nitric oxide** donor compn. and method for treatment of anal disorders)

L7 ANSWER 27 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:600059 CAPLUS
DN 121:200059
TI Diazotization reaction of nitric oxide trapped by hemoglobin
AU Sonoda, Masaru; Hashimoto, Taiju; Satomi, Akira; Miyazaki, Takashi; Ishida, Kiyoshi; Sakagishi, Yoshikatsu
CS Dep. Biochem., Saitama Med. Sch., Saitama, Japan

SO Life Sciences (1994), 55(11), PL199-PL204
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB The present study addresses to det. whether Hb within red blood cells can be utilized as a spin-trap agent for nitric oxide. The authors demonstrate the diazotization method coupled with a **gel** filtration chromatog., which is simply due to the sepn. of nitrosylHb from **nitrite, nitrate** or other low mol. nitroso-compds. in biol. systems and to the liberation of **nitric oxide** from nitrosyl heme-complexes in the acidic condition. The amt. of nitric oxide can be estd. by the difference of absorbances at 542 nm between diazo-compds. formed by Griess reagent and hemichrome by phosphoric acid. The results indicate that Hb in red cells as a spin-trap agent would be useful for monitoring nitric oxide in the circulation under the several disease states.

L7 ANSWER 28 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:570568 CAPLUS
DN 121:170568
TI The use of nitric oxide-delivering compounds for the treatment or prevention of alcoholic liver injury
IN Nanji, Amin; Stamler, Jonathan; Loscalzo, Joseph
PA Brigham and Women's Hospital, USA; New England Deaconess Hospital
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9416740	A1	19940804	WO 1994-US970	19940127
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9462327	A1	19940815	AU 1994-62327	19940127
PRAI	US 1993-12135	A	19930129		
	WO 1994-US970	W	19940127		

AB Nitric oxide-delivering compds., e.g. S-nitrosothiols, are administered to an individual for the treatment or prevention of liver disease induced by ingestion of alc., or exposure to pharmacol. agents or industrial toxins. In addn. alc.-induced liver disease may also be prevented by administering a therapeutically effective amt. of either arginine, an arginine analog, or a nitric oxide-delivering compd., in combination with an alc. beverage which is to be consumed by an individual. Rats were fed either corn oil or satd. fats with EtOH for 4 wk then sacrificed. The decrease in **nitric oxide** was directly proportional to the increase in liver pathol., e.g. the amt. of **nitrite** concn. in rats fed with satd. fats and EtOH was 17.0 as compared with 2.8 mM for those who were fed with corn oil and EtOH.
IT Pharmaceutical dosage forms
(**topical, nitric oxide**-delivering compds. in, for prevention and treatment of liver injury)

L7 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1992:467165 CAPLUS
DN 117:67165
TI A common enzyme may be responsible for the conversion of organic **nitrates** to **nitric oxide** in vascular microsomes
AU Chung, Suk Jae; Fung, Ho Leung
CS Sch. Pharm., State Univ. New York, Buffalo, NY, 14260, USA
SO Biochemical and Biophysical Research Communications (1992), 185(3), 932-7

CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
TI A common enzyme may be responsible for the conversion of organic **nitrates** to **nitric oxide** in vascular microsomes
AB The nitric oxide (NO)-generating behavior of nitroglycerin (NTG), pentaerythritol trinitrate (PEtriN), and isosorbide dinitrate (ISDN) in the microsomal prepn. of bovine coronary artery smooth muscle cells was compared. The comparative NO generating activities among these nitrates were consistent with their relative reported vasodilating activities. Consistent with previous observations with NTG, 400 .mu.M bromosulfophthalein did not affect NO generation from PEtriN and ISDN in vascular microsomes whereas 400 .mu.M 1-chloro-2,4-dinitrobenzene completely inhibited NO generation from these nitrates. **Gel** filtration chromatog. with solubilized microsomes of bovine aortic smooth muscle cells showed the primary activity of NO generation from all three **nitrates** to be eluted at about 200 kD, consistent with that found with solubilized microsomes from the bovine coronary artery microsomes. These results suggest that org. nitrates may be converted to NO by one common enzyme in vascular microsomes.
ST vascular microsome enzyme **nitrate nitric oxide** ; vasodilator **nitrate nitric oxide** forming enzyme
IT **Nitrates**, biological studies
RL: BIOL (Biological study)
(metab. of org., by **nitric oxide**-forming enzyme in vascular smooth muscle microsome, vasodilator action in relation to)
IT Blood vessel, composition
(**nitric oxide**-forming enzyme of microsome of smooth muscle of, vasodilator action of org. **nitrates** in relation to)
IT Microsome
(**nitric oxide**-forming enzyme of, of vascular smooth muscle, vasodilator action of org. **nitrates** in relation to)
IT 10102-43-9, **Nitric oxide**, biological studies
RL: FORM (Formation, nonpreparative)
(formation of, from org. **nitrates** in vascular smooth muscle microsome, enzyme catalyzing, vasodilator action in relation to)

L7 ANSWER 30 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1991:97134 CAPLUS
DN 114:97134
TI Formation of a potent respiratory inhibitor at nitrite reduction by nitrite reductase isolated from the bacterium Paracoccus denitrificans
AU Kucera, Igor; Skladal, Petr
CS Fac. Sci., Masaryk Univ., Brno, 611 37, Czech.
SO Journal of Basic Microbiology (1990), 30(7), 515-22
CODEN: JBMIEQ; ISSN: 0233-111X
DT Journal
LA English
AB A new method of dissimilatory **nitrite** reductase (cytochrome cd1) isolation from the periplasmic fraction of anaerobically grown cells of the bacterium P. denitrificans was developed, using ionex and **gel** permeation chromatog. with FPLC system. In expts. with isolated enzyme, it was shown that through a **nitrite** redn. catalyzed by this enzyme, a substance (presumably **nitric oxide**) was formed which at submicromolar concns. inhibited terminal cytochrome oxidase of the respiratory chain of the same bacterium. These results help to explain formerly obsd. sensitivity of bacterial oxidase activity to NO2- and the mechanism of switching the electron flow from O2 to nitrogen terminal acceptors.

IT 10102-43-9, **Nitric oxide**, biological studies
RL: BIOL (Biological study)
(respiratory inhibitor formation during **nitrite** reductase purifn. from Paracoccus denitrificans periplasm in relation to)

L7 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1989:624451 CAPLUS
DN 111:224451
TI Nanogram nitrite and nitrate determination in environmental and biological materials by vanadium(III) reduction with chemiluminescence detection
AU Braman, Robert S.; Hendrix, Steven A.
CS Dep. Chem., Univ. South Florida, Tampa, FL, 33620, USA
SO Analytical Chemistry (1989), 61(24), 2715-18
CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA English
AB **Nitrite** in environmental water samples is reduced at room temp. to **nitric oxide** in acidic medium contg. vanadium(III). Nitrate is also rapidly reduced after heating to 80-90.degree.. Nitric oxide is removed from the reaction soln. by scrubbing with helium carrier gas and is detected by means of a chemiluminescence NOx analyzer. Nanogram detection limits are obtained. The method has the advantage of not requiring highly acidic solns. for nitrate redn. and has been applied to the anal. of a variety of environmental waters, sediment, plant materials (including cigarettes), and human urine and blood serum.
IT Beer
Cream substitutes
(**nitrate** and **nitrite** detn. in, by vanadium(III) redn. and chemiluminescence detection)

L7 ANSWER 32 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-667219 [65] WPIDS
CR 2002-256584 [30]; 2003-017560 [01]; 2003-874639 [81]
DNN N2004-528424 DNC C2004-238471
TI Implantable sensor for implantation within a blood vessel to monitor glucose levels has sensing surface spaced radially inward from a support side contacting the vessel wall, with a layer on the surface to minimize formation of thrombus.
DC A96 B04 D16 P31 S05
IN MOSTOWFI, D F; SILVER, J H
PA (MOST-I) MOSTOWFI D F; (SILV-I) SILVER J H
CYC 1
PI US 2004176672 A1 20040909 (200465)* 50
ADT US 2004176672 A1 CIP of US 2000-571702 20000515, CIP of US 2001-41036 20011108, CIP of US 2002-217202 20020809, US 2004-758495 20040115
FDT US 2004176672 A1 CIP of US 6442413
PRAI US 2004-758495 20040115; US 2000-571702 20000515; US 2001-41036 20011108; US 2002-217202 20020809
AB US2004176672 A UPAB: 20041011
NOVELTY - Implantable sensor (10) for implantation within a blood vessel comprises a sensor (56) carried by a support (18), with a sensing surface spaced radially inward from the support side contacting the vessel wall. The sensing surface includes a layer that minimizes the formation of thrombus. The layer comprises an anticoagulant or hydrogel or releases a pharmacological agent that inhibits cell proliferation or migration.
DETAILED DESCRIPTION - Implantable sensor (10) for implantation within a blood vessel comprises a sensor (56) carried by a support (18), with a sensing surface spaced radially inward from the support side contacting the vessel wall. The sensing surface includes a layer that minimizes the formation of thrombus. The layer comprises an anticoagulant or hydrogel or releases a pharmacological agent that inhibits cell proliferation or migration. The sensor contains an outer analyte permeable

membrane and an enzyme **gel** layer. The sensor is used to monitor glucose levels or detect **nitric oxide**.

An INDEPENDENT CLAIM is included for a method for retrieving the implantable sensor on the support.

USE - To detect nitric oxide or nitric oxide metabolite in the blood vessel (claimed). For monitoring glucose levels in a body vessel, to be delivered to a patient's vascular system preferably transluminally via the support (e.g. catheter, enlargeable frame, expandable tubular body, balloon expandable stent or self-expandable stent), for monitoring a property of blood.

ADVANTAGE - The sensing surface is positioned radially inward from the vessel wall by a sufficient distance that the blood flow shear rate at the sensing surface substantially delays obstruction of the sensing surface. The shear rate at the sensor/blood interface is sufficient to minimize the thickness of the formed thrombus layer. Thus, significant tissue deposition or encapsulation due to potential fibrotic reactions is minimized, and transport of glucose to the sensor is not altered over time. The sensor provides useful blood glucose readings for an extended period of time, without material interference from thrombus formation, embolization or other foreign body response.

DESCRIPTION OF DRAWING(S) - The figure shows a partial cut-away view of a stent sensor device surrounded by a sheath.

implantable sensor device 10
stent wall 18
sheath 52
sensor 56
conductors. 57
Dwg.2/18

TECH UPTX: 20041011

TECHNOLOGY FOCUS - POLYMERS - The hydrogel is poly(ethylene glycol), poly(N-vinyl pyrrolidone) or poly(hydroxyethylmethacrylate). The anticoagulant is heparin.

TECHNOLOGY FOCUS - BIOLOGY - Preferred Sensor: Enzyme is selected from glucose dehydrogenase, lactate oxidase and cholesterol oxidase. The sensor further comprises a transmitter on the support, for transmitting information from the sensor to an external receiver. An inductive link supplies power to the transmitter. The sensor further comprises a battery carried by the support and a tubular sheath on the tubular body. The sensor to detect **nitric oxide** comprises an ion-selective electrode, selected from amperometric, porphyrinic and microchip electrodes. The enzyme **gel** layer comprises **nitrate** reductase. The method for retrieving an implantable sensor on a support comprises positioning a catheter with a first clip so that the first clip is adjacent to the sensor, inflating a balloon attached to the catheter so that the first clip is forced around the sensor, deflating the balloon, inflating a second balloon so that the sensor is separated from the support, and deflating the second balloon. The sensor is bonded to the support by a degradable material.

TECHNOLOGY FOCUS - ELECTRONICS - Preferred Sensor: The sensor is a pressure sensor, flow sensor, an optode, an ion selective electrode, a pH electrode or an oxygen electrode.

L7 ANSWER 33 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-220128 [21] WPIDS
DNC C2003-055912
TI Method for lowering ocular hypertension involves administering a eye drop containing a combination of nitric oxide releasing agent and a cyclic guanosine-3',5'-monophosphate specific phosphodiesterase type 5 inhibitor.
DC B03 B05 D16
IN SHAHINPOOR, M; SHAHINPOOR, P; SOLTANPOUR, D
PA (SHAH-I) SHAHINPOOR M

CYC 1
PI US 2002168424 A1 20021114 (200321)* 6
ADT US 2002168424 A1 US 2002-64627 20020731
PRAI US 2002-64627 20020731
AB US2002168424 A UPAB: 20030328
NOVELTY - Method for lowering ocular hypertension involves administering a **topical** ophthalmic eye drop or ointment containing a combination (wt.%) of **nitric oxide** (NO) releasing agent or NO donor and a cyclic guanosine-3',5'-monophosphate (c-GMP) specific phosphodiesterase type 5 (PDE5) inhibitor.

ACTIVITY - Hypotensive; Ophthalmological.

MECHANISM OF ACTION - Cyclic guanosine-3',5'-monophosphate (c-GMP) enhancer; Phosphodiesterase type 5 (PDE5) production inhibitor.

USE - For the treatment of ocular hypertension (claimed) and glaucoma.

ADVANTAGE - The method can synergistically enhance the aqueous humor outflow, ocular hypotensive and blood circulation to the optic nerve and lowers intraoccular pressure.

Dwg.0/0
TECH UPTX: 20030328
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: The topical ophthalmic solution contains at least one tonicity adjusting agent, buffer, antioxidant and antimicrobial agent.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Compounds: The NO releasing agent is Organic **Nitrates** (such as nitroglycerine), O-nitrosylated compound (i.e. O-nitroso compound or organic **nitrites**), S-nitrosylated compound (i.e. S-nitroso compound or S-nitrosothiol compound e.g. glutathione), S-nitrosylated derivatives of captopril, S-nitrosylated proteins/peptides, S-nitrosylated oligosaccharides or polysaccharides, NO-notates compounds (such as piperazines 2 and diazeniumdiolates), inorganic nitroso compound (e.g. sodium nitroprusside), Sydonimines, or L-arginine (which does not release NO directly, but rather is an enzyme substrate which leads to the formation of **nitric oxide** in vivo).

L7 ANSWER 34 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2002-241699 [29] WPIDS
DNC C2002-072705
TI Treatment of sexual dysfunction e.g. male impotence involves the use of salified or non salified **nitric oxide** donor drugs or **nitrate** salts of phosphodiesterase inhibitors.
DC B05
IN DEL SOLDATO, P
PA (NICO-N) NICOX SA; (DSOL-I) DEL SOLDATO P
CYC 86
PI WO 2002011706 A2 20020214 (200229)* EN 40
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AU BA BB BG BR BZ CA CN CR CU CZ DM DZ EE GD GE HR HU ID IL IN IS JP KP KR LC LK LR LT LV MA MG MK MN MX NO NZ PL RO SG SI SK TR TT UA US UZ VN YU ZA
AU 2001091690 A 20020218 (200244)
US 2003171393 A1 20030911 (200367)
IT 1318673 B 20030827 (200374)
EP 1363628 A2 20031126 (200380) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU MC NL PT RO SE SI TR
JP 2004506619 W 20040304 (200417) 88
ADT WO 2002011706 A2 WO 2001-EP8733 20010727; AU 2001091690 A AU 2001-91690 20010727; US 2003171393 A1 WO 2001-EP8733 20010727, US 2003-333927 20030204; IT 1318673 B IT 2000-MI1847 20000808; EP 1363628 A2 EP

2001-971797 20010727, WO 2001-EP8733 20010727; JP 2004506619 W WO 2001-EP8733 20010727, JP 2002-517043 20010727

FDT AU 2001091690 A Based on WO 2002011706; EP 1363628 A2 Based on WO 2002011706; JP 2004506619 W Based on WO 2002011706

PRAI IT 2000-MI1847 20000808

TI Treatment of sexual dysfunction e.g. male impotence involves the use of salified or non salified **nitric oxide** donor drugs or **nitrate** salts of phosphodiesterase inhibitors.

AB WO 200211706 A UPAB: 20020508

NOVELTY - In the treatment of sexual dysfunction at least one of salified or non salified **nitric oxide** donor drugs, or **nitrate** salts of compounds inhibiting phosphodiesterases are used.

DETAILED DESCRIPTION - In the treatment of sexual dysfunction at least one salified or non salified **nitric oxide** donor drugs of formula A-X1-N(O)z (I), or **nitrate** salts of compounds (II) inhibiting phosphodiesterases are used.

z = 1 or 2 (preferably 2);

A = R(COXu)t;

u, t = 0 or 1;

X = O, NH or NR1c;

R1c = linear or branched 1-10C alkyl;

X1 = -(C(R17)(R18))n'-Y-(C(R19)(R20))n''-O-;

n' = 0-3;

n'' = 1-3;

R17-R20 = H, linear or branched 1-4C alkyl;

Y = heterocyclic ring of 5-6 atoms containing 1-2 N atoms (optionally containing 1 O or S atom);

R = phenyl (substituted by R1 and R2), residue of 2-((2-methyl-3-(trifluoromethyl)phenyl)amino)-3-pyridinecarboxylic) acid, -C(R2a)(R3a)-R1a, -C(R4d)(R4d')-R4, 2-methyl-3-(N-(2-pyridyl)carbamoyl)-1,1-dioxo-1,2-dihydro-1(lambda (6))-thieno(2,3-e)(1,2)thiazin-4-oxy (A1), 2-methyl-3-(N-(2-pyridyl)carbamoyl)-1,1-dioxo-1,2-dihydro-1(lambda (6))-benzo(e)(1,2)thiazin-4-oxy (A2), 1-(4-chlorobenzoyl)-5-methoxy-2-methylindol-3-ylmethyl (A3), 5-chloro-2-oxo-3-(thiophene-2-carbonyl)-2,3-dihydro-indole-1-carbonylamino (A4), 2-(6-methoxy-2-naphthyl)ethyl (A5), 5-fluoro-1-(4-methanesulfinylbenzylidene)-2-methyl-1H-inden-3-ylmethyl (A6), 2-methyl-3-(N-(5-methylthiazol-2-yl)carbamoyl)-1,1-dioxo-1,2-dihydro-1(lambda (6))-benzo(e)(1,2) thiazin-4-oxy (A7), 6-chloro-2-methyl-3-(N-(2-pyridyl)carbamoyl)-1,1-dioxo-1,2-dihydro-1(lambda (6))-thieno(2,3-e)(1,2)thiazin-4-oxy (A8), cis-2-(N,N-dimethylaminomethyl)-1-(3-methoxyphenyl)cyclohexyloxy (A9), 4-acetamidophenoxy (A10) or a groups of formula (i)-(iv);

R1 = OCOR3;

R3 = methyl, ethyl, linear or branched 3-5C alkyl or a residue of an heterocycle (containing only one ring having 5 or 6 atoms which can be aromatic, partially or totally hydrogenated containing at least one heteroatom selected from O, N or S);

R2 = H, OH, halogen, linear or branched 1-4C alkyl, linear or branched 1-4C alkoxy, linear or branched 1-4C perfluoroalkyl (preferably trifluoromethyl), nitro, amino, mono- or di-(1-4C) alkylamino;

n = 0-1;

R25, R26 = H, linear or branched 1-3C alkyl;

R21-R24 = H, linear or branched (1-6C) -alkyl or -alkoxy, Cl, F or Br;

R2a, R3a = H, linear or branched optionally substituted 1-12C alkyl or allyl;

R1a = R31-1,4-phenylene-C(O)-T, Ar-C(O)-T', a group of formula (v), 4-(thiophene-2-carbonyl)phenyl, 4-(1-oxo-2,3-dihydroisoindol-2-yl)phenyl, 3-phenoxyphenyl, 1,8-diethyl-1,3,4,9-tetrahydropyrano(3,4-b)indol-1-yl, 2-fluoro-1,1'-biphenyl-4-yl, 2-(4-methylbenzoyl)-1-methyl-1H-pyrrol-5-yl, 4-phenylbenzoylmethyl, 10H-9-oxa-1-azaanthracen-6-yl, 11-oxo-10H-dibenzo(b,f)oxepin-2-yl, 4-(2-oxocyclohexylidenemethyl)phenyl,

4-benzyl-1-ethyl-1,3,4,4a,9,9a-hexahydropyrano(3,4-b)indol-1-yl, 4-(4-chlorophenyl)-1-(4-fluorophenyl)-1H-pyrazol-3-yl, 10-oxo-11H-dibenzo(b,f)thiepin-2-yl or 3,4-bis(4-methoxyphenyl)isoxazol-5-yl, 2-amino-3-(4-bromobenzoyl)phenyl;

T = 1,3-phenylene (substituted on 2-position by R32);

T' = thiophene-2,5-diyl;

R31 = H or SR33;

R33 = linear or branched 1-4C;

R32 = H or OH;

R40 = H, linear or branched 1-6C alkyl, 1-6C alkoxycarbonyl linked to a 1-6C alkyl, 1-6C carboxyalkyl or 1-6C alkanoyl (optionally substituted by halogens, (halo)benzyl or (halo)benzoyl);

R41 = H, halogen, OH, CN, 1-6C alkyl (optionally containing OH group), 1-6C alkoxy, acetyl, benzyloxy, SR42, 1-3C perfluoroalkyl, 1-6C carboxyalkyl (optionally containing OH, NO2 or amino), sulfamoyl, di-(1-6)alkyl sulfamoyl or difluoro(1-3C)alkyl sulfonyl;

R42 = 1-6C alkyl;

R41a = halogen, CN, 1-6C alkyl (containing at least one OH), 1-6C alkoxy, acetyl, acetamido, benzyloxy, SR33, 1-3C perfluoroalkyl, hydroxy, 1-6C carboxyalkyl, NO2, amino, mono- or di-(1-6C)alkyl-amino, sulfamoyl, di-(1-6)alkyl sulfamoyl or di-fluoroalkyl sulfamoyl;

R41+R41a = 1-6C alkylenedioxy;

Ar = (hydroxy)phenyl (optionally mono- or poly-substituted by halogen, alkanoyl or 1-6C alkoxy), 1-6C (preferably 1-3C)trialkyl, cyclopentyl, cyclohexyl, cycloheptyl, heteroaryl (preferably thienyl), furyl (optionally containing OH) or pyridyl;

R4d, R4d' = H, linear or branched 1-6C alkyl (preferably 1-2C alkyl) or difluoro(1-6C)alkyl (preferably difluoromethyl); or

R4d+R4d' = methylene;

R4 = 4-(2-oxocyclopentylmethyl)phenyl, group of formula (vi) or R8-1,4-phenylene;

R10 = 1-6C alkyl, 3-7C cycloalkyl, 1-7C alkoxymethyl, 1-3C trifluoroalkyl, vinyl, ethynyl, halogen, 1-6C alkoxy, difluoro(1-7C)alkoxy, 1-7C alkoxymethyloxy, 1-7C alkylthio methyloxy, 1-7C alkyl methylthio, cyano, difluoromethylthio, phenyl or phenylalkyl (optionally substituted by 1-8C alkyl);

R8 = optionally branched 2-5C alkyl, 2-3C alkyloxy, allyloxy, phenoxy, phenylthio or 5-7C cycloalkyl (optionally substituted in 1 position by 1-2C alkyl);

R7 = H, linear or branched 1-4C alkyl; and

R7a = R7, linear or branched 1-4C alkoxy, Cl, F or Br (on the ortho, meta or para position);

provided that:

(i) when R25 is H, R26 is benzyl;

(ii) when at least one of R2a or R3a is allyl, then the other is H (preferably R2a is H or 1-4C alkyl, and R3a is H);

(iii) when R is (A4), then t is 0;

(iv) when R is (A1) or (A2), then t is 0 or 1 and u is 0;

(v) when R is (A5), then t and u are 0 or 1;

(vi) when R is (A3) or (A6), then A is RCOO, t and u are 1;

(vii) when R is (A7) it is a meloxicam residue;

(viii) when R is (A2) with -CH(CH3)OCOC2H5, the residue is ampiroxicam;

(ix) when R is (A8) and the valence is saturated with H, then the residue is derived from lornoxicam;

(x) when R is (A10) and the valence is saturated by H, the compound is paracetamol; and

(xi) when R is (A9) and the valence is saturated by H, the compound is tramadol.

An INDEPENDENT CLAIM is also included for a pharmaceutical formulation containing a salt of (I) and/or (II).

ACTIVITY - Vasotropic.

MECHANISM OF ACTION - Myorelaxant.

White New Zealand rabbits were sacrificed, cavernous body and aorta specimens were taken and prepared for the determination of in vitro myorelaxing activity as described by J. Jeremy, Br. J. Urology, 79, 958-963, (1997). 2-(Acetyloxy)benzoic acid-6-(nitroxymethyl)-2-methylpyridyl ester hydrochloride (NC X 4050), sildenafil nitrate (test compounds) and sodium nitroprussate (comparative) at 1 micro M were tested. The myorelaxing effect of the cavernous body/aorta for (NC X 4050), sildenafil nitrate and comparative were found to be 80/80, 100/20 and 50/100 with a power ratio of 1, 5 and 0.5 respectively.

USE - In the treatment of sexual dysfunction (claimed) (particularly male impotence and female sexual dysfunction).

ADVANTAGE - The salts of (I) and (II) have a low pressure effect. Unlike sildenafil citrate, (II) can also be used for the impotence treatment of cardiopathic patients.

Dwg.0/0

TECH UPTX: 20020508

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Salts: When the formulations are used for **topical** application salts other than **nitrates** (preferably oxalate, tartrate, maleate, succinate, citrate, glycinate, lysinate, chloride, sulfate or phosphate) of (II) can also be used.

TT TT: TREAT SEX DYSFUNCTION MALE IMPOTENCE SALT NON SALT **NITRIC OXIDE** DONOR DRUG **NITRATE** SALT PHOSPHODIESTERASE INHIBIT.

L7 ANSWER 35 OF 43 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1998-044887 [05] WPIDS
DNC C1998-015115
TI **Topical** composition for the relief of erectile dysfunction - comprises aminophylline, co-dergocrine mesylate, isosorbide di **nitrate**, at least one **nitric oxide** releaser/carrier, and optionally testosterone.
DC B05
IN CARRUTHERS, M E
PA (MULT-N) MULTIMED LTD
CYC 1
PI GB 2314771 A 19980114 (199805)* 7
GB 2314771 B 20000906 (200044)
ADT GB 2314771 A GB 1996-13860 19960702; GB 2314771 B GB 1996-13860 19960702
PRAI GB 1996-13860 19960702
TI **Topical** composition for the relief of erectile dysfunction - comprises aminophylline, co-dergocrine mesylate, isosorbide di **nitrate**, at least one **nitric oxide** releaser/carrier, and optionally testosterone.
TT TT: **TOPICAL** COMPOSITION RELIEF DYSFUNCTION COMPRISE AMINOPHYLLINE CO METHANESULPHONATE ISOSORBIDE DI **NITRATE** ONE **NITRIC OXIDE** RELEASE CARRY OPTION TESTOSTERONE.

L7 ANSWER 36 OF 43 MEDLINE on STN
AN 2002147458 MEDLINE
DN PubMed ID: 11820854
TI The effect of local administration of N-acetylcysteine in perforated rat tympanic membrane: an experimental study in myringosclerosis.
AU Ozcan Cengiz; Polat Gurbuz; Gorur Kemal; Talas Derya Umit; Bagdatoglu Ozlen; Cinel Ismail
CS Department of Otorhinolaryngology, Mersin University, School of Medicine, Mersin, Turkey.. cengizozcan@hotmail.com
SO Pharmacological research : official journal of the Italian Pharmacological Society, (2002 Jan) 45 (1) 5-9.
Journal code: 8907422. ISSN: 1043-6618.
CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020308
Last Updated on STN: 20020623
Entered Medline: 20020621
AB Myringosclerosis (MyS) is a common sequela of acute and chronic otitis media and ventilation tube treatment of serous otitis media. We aimed to study the effect of **topical** administration of N -acetylcysteine (NAC) on MyS by assessment of otomicroscopic evaluation, lipid peroxidation and **nitric oxide** (NO) (**nitrite/nitrate**) levels in experimental myringotomized rat tympanic membrane. Thirty adult rats were used and the upper posterior quadrant of the tympanic membranes of rats was myringotomized. Thereafter, they were divided into four groups. Group I received no treatment, group II was treated with saline, groups III and IV were treated with topical NAC (0.1 ml of 6 and 12 mg ml(-1), respectively). The levels of nitrite/nitrate and malondialdehyde (MDA) were measured in serum samples. In the otomicroscopic evaluation, non-treated and saline treated ears (controls) showed extensive occurrence of myringosclerotic plaques. Groups III and IV showed fewer occurrences of sclerotic plaques. There was no significant difference between groups III and IV regarding the development of MyS. The development of myringosclerotic lesion was found to be significantly different between NAC treated groups (III and IV) and the control groups (I and II). The levels of nitrite/nitrate of both groups III and IV were significantly lower than the control groups. The levels of MDA of these groups were also significantly lower than the control group. The relationship between groups III and IV was not statistically significant for the levels of nitrite/nitrate and MDA. We conclude that the topical treatment of NAC reduces the levels of MDA and NO products in rats. These results suggest that topical NAC application may be useful for the prevention of MyS.

L7 ANSWER 37 OF 43 MEDLINE on STN
AN 2002009562 MEDLINE
DN PubMed ID: 11354794
TI Role of mitogen-activated protein kinase in the inhibition of myocardial hypertrophy by nitric oxide in renovascular hypertensive rats.
AU Lu W; Liu P Q; Wang T H; Gong S Z; Fu S G; Pan J Y
CS Department of Physiology, Sun Yat-Sen University of Medical Sciences, Guangzhou 510089.
SO Sheng li xue bao [Acta physiologica Sinica], (2001 Feb) 53 (1) 32-6.
Journal code: 20730130R. ISSN: 0371-0874.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 200210
ED Entered STN: 20020121
Last Updated on STN: 20021026
Entered Medline: 20021025
AB The aim of this study was to examine the effects of L-arginine, a **nitric oxide** (NO) precursor, on protein expression of endothelial **nitric oxide** (eNOS), **nitrite/nitrate** content, protein expression of mitogen-activated protein kinase phosphatase-1 (MKP-1) and the activity of mitogen-activated protein kinase (MAPK) in cardiac tissues in renovascular hypertensive rats (RHR). The Goldblatt renovascular hypertensive model was established by two-kidney one clip method. The rats were divided into four groups, respectively treated with 50, 150 and 450 mg/kg L-arginine and 150 mg/kg

L-arginine plus 10 mg/kg L-NAME (an eNOS inhibitor) (i.p.). Another group did not receive specific treatment from the 5th week after renal artery constriction. Control group was sham-operated. Mean arterial blood pressure (MABP) and the ratio of left ventricular weight to body weight (LVW/BW) were measured 8 weeks after treatment. eNOS protein expression, **nitrite/nitrate** content, MKP-1 protein expression and MAPK activity in cardiac tissues were detected using Western blot analysis, enzyme-reduction method and substrate in-**gel** kinase assay, respectively. It was found that L-arginine significantly inhibited the increase of MABP and LVW/BW, attenuated the activity of MAPK, increased protein expression of eNOS and MKP-1 and potentiated production of NO in cardiac tissue with the most effective dosage of 150 mg/kg, and these effects of L-arginine could be inhibited by L-NAME. These results suggest that MKP-1 may play an important role in the NO-induced inhibition of myocardial hypertrophy. The anti-hypertrophic effects of L-arginine may involve increase of eNOS protein expression and NO production, potentiation of MKP-1 protein expression, and inhibition of MAPK activity in the cardiac tissue of RHR.

L7 ANSWER 38 OF 43 MEDLINE on STN
AN 1999238277 MEDLINE
DN PubMed ID: 10223761
TI Nitroglycerin ointment for anal fissures: effective treatment or just a headache?.
CM Comment in: Dis Colon Rectum. 1999 Aug;42(8):1106. PubMed ID: 10458141
AU Hyman N H; Cataldo P A
CS Department of Surgery, University of Vermont College of Medicine, Burlington 05405, USA.
SO Diseases of the colon and rectum, (1999 Mar) 42 (3) 383-5.
Journal code: 0372764. ISSN: 0012-3706.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199905
ED Entered STN: 19990525
Last Updated on STN: 20000229
Entered Medline: 19990513
AB PURPOSE: **Topical nitrates** have been shown to cause **nitric oxide**-mediated relaxation of the internal anal sphincter. Previous reports have suggested initial efficacy in the treatment of anal fissures. The aim of this study was to assess the longer-term usefulness of this treatment. METHODS: Thirty-three patients with an anal fissure were treated with topical 0.3% nitroglycerin ointment, applied to the anoderm three times per day and after bowel movements. Patients were followed up by office visits and telephone calls until symptoms were completely resolved or treatment was noted to be ineffective or intolerable. RESULTS: Thirty-three patients were treated, 16 with acute fissures, and 17 with chronic fissures. Nitroglycerin was effective in 9 of 16 acute fissures (56%), and 7 of 17 chronic fissures (41%). Even when effective, 75% of patients reported an adverse reaction. CONCLUSIONS: Topical nitroglycerin was only effective in approximately one-half of patients with an anal fissure. There was a very high incidence of adverse reactions. In our experience nitroglycerin more often causes a headache than treats the symptoms of anal fissure.

L7 ANSWER 39 OF 43 MEDLINE on STN
AN 1999113027 MEDLINE
DN PubMed ID: 9893176
TI Evaluation of linear polyethyleneimine/nitric oxide adduct on wound repair: therapy versus toxicity.
AU Bauer J A; Rao W; Smith D J

CS Department of Chemistry, University of Akron, Ohio 44325-3601, USA.
SO Wound repair and regeneration : official publication of the Wound Healing Society [and] European Tissue Repair Society, (1998 Nov-Dec) 6 (6) 569-77. Journal code: 9310939. ISSN: 1067-1927.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990311
Last Updated on STN: 19990311
Entered Medline: 19990222
AB A full-thickness wound model was used to evaluate the effects of a **topically** applied polyethyleneimine-based **nitric oxide** donor on wound repair in aged rats. Polymer applications were applied over a 10-day period on days 0, 2, 4, 6, and 8 comparing treatment (linear polyethyleneimine-nitric oxide) and control groups (linear polyethyleneimine). Urinary **nitrate** excretion was quantified as a measure of **nitric oxide** released. The **nitric oxide** released from the linear polyethyleneimine-**nitric oxide** group was significant compared with controls ($p </= 0.001$), with a maximal **nitrate** level of 40 micromol on day 1 and an average sustained delivery of 34 micromol/day for the remainder of the study. Wound closure was examined using a computer-based video-imaging analysis system. The wounds of both the linear polyethyleneimine- nitric oxide treatment and linear polyethyleneimine control groups exhibited minimal wound closure; however, the wound closure of the treatment group was significant as compared with the control group ($p </= 0.05$). A phosphate- buffered saline solution-wounded control was performed that showed cleaner and faster healing wounds, similar to normal healing, than either of the polymer application groups. The histological data showed very little wound healing, on a cellular level, implicating the linear polyethyleneimine-nitric oxide as well as the carrier compound as contributing to the adverse tissue reactions that occurred in the wound bed. Thus, we report the toxic effects of a polyethyleneimine-based compound, as well as the toxic effects of sustained delivery of excess levels of nitric oxide on the wound- repair process. Our findings suggest that there exists indeterminate parameters between therapy and toxicity of nitric oxide delivery to wounds.

L7 ANSWER 40 OF 43 MEDLINE on STN
AN 1998215077 MEDLINE
DN PubMed ID: 9555794
TI A randomized trial of acidified **nitrite cream** in the treatment of tinea pedis.
AU Weller R; Ormerod A D; Hobson R P; Benjamin N J
CS Department of Dermatology, Aberdeen Royal Infirmary, Foresterhill, United Kingdom.
SO Journal of the American Academy of Dermatology, (1998 Apr) 38 (4) 559-63. Journal code: 7907132. ISSN: 0190-9622.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199805
ED Entered STN: 19980514
Last Updated on STN: 19980514
Entered Medline: 19980505
TI A randomized trial of acidified **nitrite cream** in the

treatment of tinea pedis.

AB BACKGROUND: Nitric oxide is continually released from normal skin and has antimicrobial effects. An acidified **nitrite cream** releases supraphysiologic concentrations of **nitric oxide** and is fungicidal in vitro. OBJECTIVE: The purpose of this study was to assess the efficacy of an acidified **nitrite cream** as treatment for tinea pedis. METHODS: Sixty patients were recruited with both a clinical diagnosis of tinea pedis and hyphae identified on direct microscopy; they were randomly placed into an active group treated with twice-daily application of a mixture of 3% salicylic acid in aqueous **cream** and 3% **nitrite** in aqueous **cream** for 4 weeks and a control group treated with 3% salicylic acid in aqueous **cream** and aqueous **cream** alone. Nineteen patients completed the trial in the active group and 16 patients in the control group. Mycologic cure (negative results on microscopy and culture) and clinical improvement were measured at 0, 2, and 4 weeks and after a 2-week interval with no treatment. RESULTS: At the end of the treatment period, 18 of the 19 patients in the active group were mycologically cured as were 11 of 16 in the control group ($p = 0.042$). Two weeks after the cessation of treatment, 13 of 19 patients in the active group were mycologically cured and 5 of 16 in the control group ($p = 0.028$). The initial clinical scores in the active and control groups were 8.1 and 8.19 (two-tailed $p = 0.95$). At 4 weeks they were 1.66 and 6.0 (two-tailed $p = 0.002$) and after 2 weeks with no treatment 1.45 and 7.4 (two-tailed $p < 0.0002$). CONCLUSION: Acidified nitrite is effective therapy for tinea pedis.

L7 ANSWER 41 OF 43 MEDLINE on STN
AN 97457965 MEDLINE
DN PubMed ID: 9314309
TI **Nitric oxide** production in burns: plasma **nitrate** levels are not increased in patients with minor thermal injuries.
AU Harper R; Parkhouse N; Green C; Martin R
CS Blond McIndoe Centre, Queen Victoria Hospital, West Sussex, United Kingdom.
SO Journal of trauma, (1997 Sep) 43 (3) 467-74.
Journal code: 0376373. ISSN: 0022-5282.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199710
ED Entered STN: 19971105
Last Updated on STN: 19971105
Entered Medline: 19971021
TI **Nitric oxide** production in burns: plasma **nitrate** levels are not increased in patients with minor thermal injuries.
AB BACKGROUND: Recent studies have suggested that adults who sustain burns of less than 15% total body surface area display elevated plasma **nitrate** levels, indicating increased production of **nitric oxide**. The present study was initiated to confirm whether plasma nitrate is elevated in minor burn injury and, if so, whether it heralds the onset of a systemic inflammatory response to that injury. METHODS: Plasma samples were taken from 98 control and 10 burns patients. RESULTS: The mean plasma nitrate level for nine burns patients with a mean total body surface area burnt of 7.65% (range, 4-15%) was 42.83 micromol/L on day 1. This was not significantly different from that of a control population of 98 preoperative plastic surgery patients: 36.91 micromol/L ($p = 0.162$). Eight of 10 burns patients showed a decrease in plasma nitrate to 27.47 micromol/L by day 3 ($p = 0.046$). Elevated nitrate levels were seen in 2 of 10 burns patients. One had concurrent smoke-inhalation

injury preceding multiple organ dysfunction, and one was treated with a **cream** containing cerium **nitrate** (Flammacerium, Duphar Laboratories, Southhampton, United Kingdom). CONCLUSIONS: For patients who sustain minor burns, plasma levels of nitrate decrease from those of mean normal controls with time unless there is multiple organ dysfunction or the patient receives extraneous nitrate.

L7 ANSWER 42 OF 43 MEDLINE on STN
AN 92345240 MEDLINE
DN PubMed ID: 1379071
TI Mechanistic probes of N-hydroxylation of L-arginine by the inducible nitric oxide synthase from murine macrophages.
AU Pufahl R A; Nanjappan P G; Woodard R W; Marletta M A
CS Interdepartmental Program in Medicinal Chemistry, College of Pharmacy, University of Michigan, Ann Arbor 48109-1065.
NC CA 50414 (NCI)
T32 GM07767 (NIGMS)
SO Biochemistry, (1992 Jul 28) 31 (29) 6822-8.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199208
ED Entered STN: 19920911
Last Updated on STN: 19970203
Entered Medline: 19920828
AB NG-Hydroxy-L-arginine, [15N]-NG-hydroxy-L-arginine, and NG-hydroxy-NG-methyl-L-arginine were used as mechanistic probes of the initial step in the reaction catalyzed by nitric oxide synthase isolated from murine macrophages. NG-Hydroxy-L-arginine was found to be a substrate for nitric oxide synthase with a Km equal to 28.0 microM, yielding nitric oxide and L-citrulline. NADPH was required for the reaction and (6R)-tetrahydro-L-biopterin enhanced the initial rate of nitric oxide formation. The stoichiometry of NG-hydroxy-L-arginine loss to L-citrulline and **nitric oxide** (measured as **nitrite** and **nitrate**) formation was found to be 1:1:1. NG-Hydroxy-L-arginine was also observed in small amounts from L-arginine during the enzyme reaction. Studies with [15N]-NG-hydroxy-L-arginine indicated that the nitrogen in nitric oxide is derived from the oxime nitrogen of [15N]-NG-hydroxy-L- arginine. NG-Hydroxy-NG-methyl-L-arginine was found to be both a reversible and an irreversible inhibitor of nitric oxide synthase, displaying reversible competitive inhibition with K(i) equal to 33.5 microM. As an irreversible inhibitor, NG-hydroxy-NG-methyl-L-arginine gave kinact equal to 0.16 min-1 and KI equal to 26.5 microM. This inhibition was found to be both time- and concentration-dependent as well as showing substrate protection against inactivation. **Gel** filtration of an NG-hydroxy-NG-methyl-L-arginine-inactivated **nitric oxide** synthase failed to recover substantial amounts of enzyme activity.

L7 ANSWER 43 OF 43 MEDLINE on STN
AN 84148959 MEDLINE
DN PubMed ID: 6670357
TI Purification and characterization of a dissimilatory nitrite reductase from the phototrophic bacterium Rhodopseudomonas palustris.
AU Preuss M; Klemme J H
SO Zeitschrift fur Naturforschung. Section C: Biosciences, (1983 Nov-Dec) 38 (11-12) 933-8.
Journal code: 7801143. ISSN: 0341-0382.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 198403
ED Entered STN: 19900319
Last Updated on STN: 20000303
Entered Medline: 19840327

AB A dissimilatory nitrite reductase from the facultatively phototrophic bacterium, Rhodopseudomonas palustris strain 1a1 was studied. A basic level of the enzyme (10-50 mU/mg protein) was measured in dark, aerated and anaerobic, photosynthetic cultures. A marked derepression of enzyme synthesis occurred under conditions of oxygen limitation (200-300 mU/mg protein). The addition of nitrite (or nitrate) to the culture medium had only a slight effect on the maximal nitrite reductase titer of cells. The enzyme was purified from photosynthetically grown cells by precipitation with ammonium sulfate, gel filtration through Sepharose 6B and repeated chromatography on DE 52-cellulose. As estimated by **gel** filtration, the **nitrite** reductase had a molecular weight of about 120 000 +/- 12 000 and yielded only one band (mol. wt. of about 68 000 +/- 7000) in SDS-**gel** electrophoresis. The isoelectric point of the enzyme was at pH 5.1. **Nitric oxide** (NO) was identified as the reaction product of **nitrite** reduction. The enzyme also exhibited cytochrome c-oxidase activity and was active with chemically reduced viologen dyes, FMN and cytochrome c as electron donors. Highly purified nitrite reductase preparations contained 10 mol% of a c-type cytochrome. Trace metal analyses indicated the presence of Cu in the enzyme. Consistent with the detection of Cu was the finding that the Cu-chelator, diethyldithiocarbamate, strongly inhibited the nitrite reductase.